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Attorney Docket No. 10517-700.US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appl. No.	:	10/523,857	Confirmation No.:	7154
Applicant	:	Ross E. MANTLE		
Filing Date	:	May 11, 2005		
Title	:	Device for the Extravascular Recirculation of Liquid in Body Cavities		
Group Art Unit	:	3761		
Examiner	:	Philip R. WIEST		
Docket No.	:	10517-700.US0		
Customer No.	:	66854		

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 41.37

MailStop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Sir:

Appellant submits this brief in accordance with the provisions of 37 C.F.R. § 41.37 in response to the Final Rejection mailed January 8, 2008. Appellant's Notice of Appeal was filed March 5, 2008. This Appeal Brief is therefore timely filed.

The filing fee for this document is being paid via EFS. Please charge any deficit in these fees to Deposit Account No. 50-4050.

I. REAL PARTY IN INTEREST

The real party in interest is Ross E. Mantle, sole inventor named herein. No assignment has been made.

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF CLAIMS

In the current application under appeal, claims 1-13 and 18-37 are pending, and claims 14-17 are cancelled. The rejection of claims 1-13 and 18-37 is appealed herein.

IV. STATUS OF AMENDMENTS

Appellant has submitted no amendments after the final rejection. All amendments prior to the close of prosecution on the merits have been entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 1 recites an apparatus for modulating the temperature and pressure within a body cavity by means of recirculation of a biological or biocompatible liquid within the cavity, but outside of blood vessels, including (a) a first pump means for infusing liquid at a controlled temperature and flow rate into the cavity; (b) means for monitoring the temperature within the cavity; (c) means for monitoring the pressure within the cavity; and (d) second pump means for withdrawing liquid at a controlled flow rate from the cavity.

Support for the first pump means for infusing liquid at a controlled temperature and flow rate into the cavity may be found at least on page 7, lines 17-23;[1] page 8, lines 5-7 and 25-29; page 9, lines 1-3 and 9-19; page 11, lines 1-7; page 12, lines 5-17; page 13, lines 24-27; page 14, lines 5-7; page 15, lines 3-21; page 16, line 26 to page 17, line 17; page 17, line 26 to page 18, line 14; page 20, line 8, to page 22, line 18; chamber 7, baffles 104-108, pump 16, tubing 130, catheter 8, inflow barrel 19, thermocouple 105, antenna 107, regulator 15, heater/cooler 14,

[1] Page and line references are made to the specification as filed, not as published.

antenna 142, and computer 141 in Figure 1; and insertion tip 8A, primary catheter 8 and orifices 20 in Figures 2A and 2B.

Support for the means for monitoring the temperature within the cavity may be found at least on page 8, lines 9-12; page 9, lines 9-10; page 11, lines 7-11, 15-22 and 30-32; page 12, lines 1-2; page 14, line 28 to page 15, line 3; page 17, lines 17-22; and sensor package 21, T-type thermocouple wire 172/173, wires 150, sensor 102, antenna 103, antenna 142 and computer 141 in Figure 1.

Support for the means for monitoring the pressure within the cavity may be found at least on page 8, lines 9-12; page 9, lines 9-10; page 11, line 7-15 and 19-22; page 17, lines 17-19; sensor package 21A, wires 151, antenna 142 and computer 141 in Figure 1; page 14, line 28 to page 15, line 3; and 4-wire strain gauge 171 in Figure 1.

Support for the second pump means may be found at least on page 7, lines 17-23; page 8, line 7-9; page 9, lines 5-7 and 9-15; page 11, lines 1-7; page 12, lines 18-20; page 14, lines 5-7; page 15, line 12 to page 16, line 24; page 17, lines 3-22; pump 5, catheter 1, tubing 101, burette 2, tubing 130, pump 134, line 132, control line 191; catheter 8, outflow lumen 18 in Figure 1; and insertion tip 8A, primary catheter 8 and orifices 20 in Figure 2A.

Independent claim 18 recites an apparatus for modulating introduction and removal of a liquid within a cavity of a patient's body, the cavity comprising a cavity outside of blood vessels, with the apparatus including: a catheter configured for insertion into the cavity and introduction and removal of liquid from the cavity; one or more sensors positionable in the patient's body so as to sense a condition of liquid in the cavity; and a controlled pumping system operatively coupled to both the catheter and the one or more sensors, the controlled pumping system configured to control introduction and removal of liquid from the cavity so as to maintain a selected liquid condition value. Support for the subject matter of this claim may be found at least at page 7, lines 17-23; page 8, lines 5-12 and 25-29; page 9, lines 1-3, 5-7 and 9-19; page 11, lines 1-22 and 30-32; page 12, lines 1-2 and 5-20; page 13, lines 24-27; page 14, lines 5-7; page 14, line 28 to page 17, line 22; page 17, line 26 to page 18, line 14; page 20, line 8, to page 22, line 18; and Figures 1, 2A and 2B.

Independent claim 28 recites a feedback-controlled apparatus for introduction and removal of a liquid within a cavity of a patient's body, the cavity comprising a cavity outside of blood vessels, the apparatus comprising: a catheter configured for insertion into the cavity and

introduction and removal of liquid from the cavity; one or more sensors positionable so as to sense a biological parameter of a patient's body; and a controlled pumping system operatively coupled to both the catheter and the one or more sensors, the controlled pumping system configured to modulate a property of the liquid in response to signals received from the one or more sensors and to maintain the biological parameter of the patient's body within a selected range. Support for the subject matter of this claim may be found at least at page 7, lines 17-23; page 8, lines 5-12 and 25-29; page 9, lines 1-3, 5-7 and 9-19; page 11, lines 1-22 and 30-32; page 12, lines 1-2 and 5-20; page 13, lines 24-27; page 14, lines 5-7; page 14, line 28 to page 17, line 22; page 17, line 26 to page 18, line 14; page 20, line 8, to page 22, line 18; and Figures 1, 2A and 2B.

Independent claim 32 recites a method of maintaining a liquid condition parameter within a body cavity other than a blood vessel within a patient's body, the method comprising: pumping liquid into the cavity; pumping liquid out of the cavity; monitoring a parameter of liquid within the cavity from a sensor disposed within the patient's body; and controlling at least one of liquid temperature, liquid pressure, and liquid flow rate in response to a liquid condition value measured in the monitoring step. Support for the subject matter of this claim may be found at least at page 7, lines 17-23; page 8, lines 5-12 and 25-29; page 9, lines 1-3, 5-7 and 9-19; page 11, lines 1-22 and 30-32; page 12, lines 1-2 and 5-20; page 13, lines 24-27; page 14, lines 5-7; page 14, line 28 to page 17, line 22; page 17, line 26 to page 18, line 14; page 20, line 8, to page 22, line 18; and Figures 1, 2A-B, 3A-C and 4 A-C.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Appellant respectfully requests the Board of Patent Appeals and Interferences to review the following grounds of rejection on appeal:

1. Whether claims 1-9 and 11-13 are patentable under 35 U.S.C. § 103(a) over Osterholm US 4,450,841 ("Osterholm") in view of Leonard US 3,927,980 and further in view of Ginsburg et al. US 6,497,721 ("Ginsburg").

2. Whether claims 18, 19, 21-23, 25-27 and 28 are patentable under 35 U.S.C. § 103(a) over Osterholm in view of Leonard and further in view of Ginsburg.[2]

[2] The Examiner's rejection did not specifically state the exact basis of the rejection of claims 25 and 26. (See Final Office Action, p. 3.) The Examiner's later remarks with respect to claims 25 and 26 suggest that the Examiner intended to include these claims in the rejection of claim 18 over Osterholm, Leonard and Ginsburg, however.

3. Whether claims 28-30 are patentable under 35 U.S.C. § 103(a) over Osterholm in view of Leonard and further in view of Ginsburg.

4. Whether claims 32-34 and 37 are patentable under 35 U.S.C. § 103(a) over Osterholm in view of Leonard and further in view of Ginsburg.

5. Whether claim 10 is patentable under 35 U.S.C. § 103(a) over Osterholm in view of Leonard and Ginsburg and further in view of Gutierrez-Collazo US 5,562,821 ("Gutierrez").

6. Whether claims 24, 31, 35 and 36 are patentable under 35 U.S.C. § 103(a) over Osterholm in view of Leonard and Ginsburg, and further in view of Maginot US 6,743,218 ("Maginot").

VII. ARGUMENTS

Appellant respectfully submits that claims 1-13 and 18-37 are in proper form and are patentable over the prior art of record.

1. Rejection of Claims 1-9 and 11-13 Over Osterholm, Leonard and Ginsburg

Osterholm describes a stroke treatment apparatus and method based on an observation that oxygenated blood may not be able to reach certain parts of the brain after a cerebrovascular accident. (Osterholm 1:64-2:3.) Osterholm therefore injects an oxygenated and nutrient-rich emulsion into a ventricle of the brain and withdraws cerebrospinal fluid from the spinal subarachnoid space or cisterna magna. (Osterholm 7:56-61; 11:15-35.) As shown in Figure 13, injection of the fluid into the patient's brain is controlled by a pump 107. As the Examiner admits, however, while Osterholm has a pump to pump fluid into the space, Osterholm's system lacks a pump to pump fluid out of the space into which it has been injected, as recited by claim 1. Furthermore, since Osterholm is not attempting to maintain the temperature of the brain, Osterholm also lacks a means of monitoring temperature within the brain as recited by claim 1.

Leonard describes an extracorporeal blood oxygenator with a suction pump 46 for removing venous blood from a vein and an arterial pump 36 for returning oxygenated blood to an artery, an anatomical cavity other than the space from which fluid was removed. In contrast, claim 1 recites an apparatus with first and second pump means infusing and withdrawing liquid from the same cavity. Furthermore, because Leonard is not concerned with maintaining the temperature or pressure of the patient's vein or artery, Leonard does not describe any means of

monitoring the temperature or pressure of the blood vessels. Claim 1, on the other hand, recites both a means for monitoring the temperature of the cavity and a means for monitoring the pressure of the cavity to which and from which liquid is infused and withdrawn.

Ginsburg describes a hypothermia therapy device that uses a heat exchange catheter inserted into a blood vessel (such as the carotid artery) to cool blood flowing to the region of the body in which hypothermia is desired (such as the brain). Ginsburg controls the temperature of the heat exchange catheter in the carotid artery by monitoring the temperature of the target tissue in the brain. (Ginsburg 13:23-14:7 and Figs. 5-6.) Ginsburg has none of the elements recited by claim 1: There is no first pump means for infusing liquid at a controlled temperature into a body cavity, no means for monitoring temperature within the cavity, no means for monitoring pressure within the cavity, and no second pump means for withdrawing liquid at a controlled flow rate from the cavity.

The Examiner's argument for the obviousness of claim 1 mischaracterizes the prior art and its teaching and fails to provide the requisite rational basis for the obviousness of that claim's subject matter required by the US Supreme Court in *KSR* as well as the USPTO's own obviousness guidelines. First, the Examiner states that "Osterholm discloses an apparatus for modulating the temperature and pressure within a body cavity . . . ." (Final Office Action, p. 3.) In fact, however, the purpose of Osterholm's stroke treatment apparatus is to provide oxygen and other nutrients to brain tissue, not to modulate the temperature and pressure of the brain.

Second, the Examiner implies that Leonard discloses the use of separate inflow and outflow pumps to supply and withdraw fluid from a body cavity and that it would have been obvious to add a second pump to the Osterholm apparatus to remove fluid from the body cavity to which Osterholm had added fluid because "[it is] obvious that pressure changes may be realized by changing the amount of fluid present within the cavity." (Final Office Action, p. 3.) In fact, however, Leonard supplies blood to an artery and withdraws blood from a vein, which are completely different parts of the body and certainly not the same body cavity. Nothing in Leonard's teaching would have suggested that adding a second pump to Osterholm's cerebrospinal fluid circulation system would have been desirable or even possible, and the Examiner's own rationale for the obviousness of the combination is nothing more than the use of hindsight to construct the claimed invention from bits and pieces of the prior art.

With respect to the recited means for monitoring temperature and means for monitoring pressure, the Examiner points to Ginsburg to support the contention that "it would have been obvious . . . to combine the apparatus of Osterholm with the use of internal pressure and temperature monitoring of Ginsburg in order to more accurately monitor the pressure and temperature inside the cavity, thereby allowing the apparatus to change the flow rate and heat transfer settings accordingly." (Final Office Action, p. 4.) Ginsburg, however, does not explicitly disclose the feature that the Examiner has admitted Osterholm lacks: means for monitoring the temperature of a cavity to which liquid is infused. Ginsburg discloses something far different: Cooling blood that is already flowing within one part of the body (without adding any fluid to that body cavity), and monitoring temperature far away from the location where the cooling is taking place. The addition of portions of the Ginsburg apparatus to the Osterholm apparatus therefore does not result in the combination of features recited by claim 1.

Furthermore, one skilled in the art would not have looked to Ginsburg to modify the Osterholm device. Osterholm introduced temperature-controlled fluid directly to the cavity of interest. Ginsburg, on the other hand, chose instead to control the temperature of blood perfusing the region of interest. Osterholm and Ginsburg took fundamentally different approaches to controlling tissue temperature, and one skilled in the art would not have looked to Ginsburg for potential modifications to the Osterholm system.

Finally, claim 1 specifically excludes modulation of temperature of blood vessels, which is exactly what Ginsburg does. Ginsburg—and the combination of Osterholm and Ginsburg—is therefore explicitly outside the scope of claim 1. For these reasons, claim 1, and claims 2-13 depending from claim 1, are patentable over Osterholm, Leonard, Ginsburg and the other prior art of record under § 103(a).

2. Rejection of Claims 18, 19, 21-23, 27 and 28 over Osterholm, Leonard and Ginsburg

The Examiner's argument with respect to independent claim 18 addresses only Osterholm's alleged controlled introduction of fluid into and out of a body cavity and appears to ignore two clear limitations recited by the claim: (1) a catheter configured for insertion into the cavity and introduction and removal of liquid from the cavity and (2) one or more sensors positionable in the patient's body so as to sense a condition of liquid in the cavity. (Final Office Action, p. 11.) These two features, in combination with the other elements recited by claim 18,

are not shown in Osterholm, Leonard or Ginsburg, and the Examiner has not offered any explanation for why these claim elements can be ignored when constructing this rejection under § 103(a). In fact, the Examiner's discussion of claim 18 never references Leonard or Ginsburg at all. The Examiner has therefore not met his burden of providing a *prima facie* basis for the obviousness of claim 18. Claim 18, and claims 19, 21-23, 27 and 28 depending from it, are therefore patentable over the prior art of record under § 103(a).

3. Rejection of Claims 28-30 Over Osterholm, Leonard and Ginsburg

As with claim 18, the Examiner's argument with respect to independent claim 28 fails to address three features explicitly recited by the claim: (1) a catheter configured for insertion into the cavity and introduction and removal of liquid from the cavity, and (2) one or more sensors positionable so as to sense a biological parameter of the patient's body and (3) a controlled pumping system operatively coupled to the catheter to modulate a property of the liquid in response to signals received from the sensors to maintain the biological parameter of the patient's body within a selected range. (Final Office Action, p. 11.) These three features, in combination with the other elements recited by claim 28, are not shown in Osterholm, Leonard or Ginsburg, and the Examiner has not offered any explanation for why these claim elements can be ignored when constructing this rejection under § 103(a). In fact, the Examiner's discussion of claim 28 never references Leonard or Ginsburg at all. The Examiner has therefore not met his burden of providing a *prima facie* basis for the obviousness of claim 28. Claim 28, and claims 29 and 30 depending from it, are therefore patentable over the prior art of record under § 103(a).

4. Rejection of Claims 32-34 and 37 Over Osterholm, Leonard and Ginsburg

The Examiner's first statement with respect to the patentability of claim 32 is not only completely erroneous, but it contradicts his earlier characterization of Osterholm. The Examiner asserts that "Osterholm does, in fact, disclose the step of pumping fluid into and out of the cavity." (Final Office Action, p. 11.) Earlier in the Office Action, however, the Examiner admitted that Osterholm lacked a pump for removing fluid from a cavity. (See Final Office Action, p. 3.)

Furthermore, the Examiner's patentability discussion omits other key elements of claim 32: (1) the step of monitoring a parameter of liquid within the cavity from a sensor

disposed within the patient's body and (2) controlling at least one of liquid temperature, liquid pressure and liquid flow rate in response to a liquid condition value measured in the monitoring step. These features, in combination with the other elements recited by claim 32, are not shown in Osterholm, Leonard or Ginsburg, and the Examiner has not offered any explanation for why these claim elements can be ignored when constructing his rejection under § 103(a).

Furthermore, since the Examiner's discussion of claim 32 never references Leonard or Ginsburg at all, the Examiner never explains why Leonard and Ginsburg, which are both drawn to methods involving blood vessels, are at all relevant to a method claim that explicitly excludes blood vessels. The Examiner has therefore not met his burden of providing a *prima facie* basis for the obviousness of claim 32. Claim 32, and claims 33, 34 and 37 depending from it, are therefore patentable over the prior art of record under § 103(a).

5. Rejection of Claim 10 Over Osterholm, Leonard, Ginsburg and Gutierrez

Gutierrez discloses a foam fractionator and has nothing to do with pumping fluid into or out of a body cavity. Claim 10 depends from claim 1 and therefore contains all of the limitations of claim 1. Gutierrez does not overcome the deficiencies of Osterholm, Leonard and Ginsburg with respect to the patentability of claim 1 under § 103(a). Claim 10 is therefore patentable over the combination of Osterholm, Leonard, Ginsburg and Gutierrez under § 103(a) for the reasons stated above with respect to claim 1.

6. Rejection of Claims 24, 31, 35 and 36 Over Osterholm, Leonard, Ginsburg and Maginot

Maginot describes a dialysis catheter (shown in Figures 7A-D) that has two lumens 42 and 44 through which blood may be withdrawn and returned from and to the superior vena cava. (Maginot 11: 59-64; 15:34-36.) Claim 24 depends from claim 18 and therefore includes all of the limitations of claim 18. Maginot does not overcome the deficiencies of Osterholm, Leonard and Ginsburg with respect to the patentability of claim 18. Claim 24 is therefore patentable over the combination of Osterholm, Leonard, Ginsburg and Maginot under § 103(a).

Claim 31 depends from claim 28 and therefore includes all of the limitations of claim 28. Maginot does not overcome the deficiencies of Osterholm, Leonard and Ginsburg with respect to

the patentability of claim 28. Claim 31 is therefore patentable over the combination of Osterholm, Leonard, Ginsburg and Maginot under § 103(a).

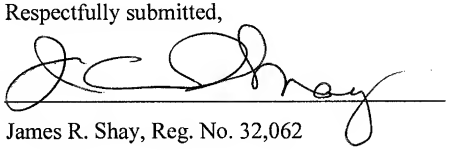
Claims 35 and 36 depend from claim 32 and therefore include all of the limitations of claim 32. Maginot does not overcome the deficiencies of Osterholm, Leonard and Ginsburg with respect to the patentability of claim 32. In fact, the Examiner has once again selected a reference directed to the placement of a device in a blood vessel to make his rejection of a method claim that specifically excludes blood vessels. Claims 35 and 36 are therefore patentable over the combination of Osterholm, Leonard, Ginsburg and Maginot under § 103(a).

CONCLUSION

For the reasons stated above, claims 1-13 and 18-37 are patentable over the prior art of record, and the rejections of those claims under 35 U.S.C. § 103 are improper and should be withdrawn. Appellant respectfully asks the Board to overturn the Examiner's rejection with instructions to allow the claims.

Respectfully submitted,

Date: May 5, 2008

By: 

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VIII. CLAIMS APPENDIX

1. (Original) Apparatus for modulating the temperature and pressure within a body cavity by means of recirculation of a biological or biocompatible liquid within the cavity, but outside of blood vessels, which comprises: (a) first pump means for infusing liquid at a controlled temperature and flow rate into the cavity; (b) means for monitoring the temperature within the cavity; (c) means for monitoring the pressure within the cavity; and (d) second pump means for withdrawing liquid at a controlled flow rate from the cavity.

2. (Original) Apparatus as claimed in claim 1, additionally comprising a dual lumen catheter insertable into said cavity, one lumen being connected to said first pump means and the second lumen being connected to said second pump means.

3. (Previously Presented) Apparatus as claimed in claim 2, comprising a further catheter insertable into said cavity to withdraw liquid from said cavity.

4. (Original) Apparatus as claimed in claim 3, in which said further catheter has associated pump means to withdraw liquid from said cavity.

5. (Original) Apparatus as claimed in claim 3, in which said further catheter has associated flow control means to regulate the flow of liquid from said cavity.

6. (Previously Presented) Apparatus as claimed in claim 1, including liquid storage means to receive liquid from said first pump means and to deliver liquid to said second pump means.

7. (Previously Presented) Apparatus as claimed in claim 6, comprising a further catheter insertable into said cavity to withdraw liquid from said cavity and in which said liquid storage means also receives liquid from said further catheter.

8. (Previously Presented) Apparatus as claimed in claim 6, in which said liquid storage means includes means to oxygenate liquid.

9. (Previously Presented) Apparatus as claimed in claim 6, in which said liquid storage means includes means to adjust the pH of the liquid.

10. (Previously Presented) Apparatus as claimed in claim 6, in which said liquid storage means includes means to separate contaminants from the liquid by foam fractionation.

11. (Previously Presented) Apparatus as claimed in claim 6, additionally comprising control means for at least one said pump means to control the operation of said pump means dependant on the output of said means for monitoring pressure and temperature within the cavity.

12. (Previously Presented) Apparatus as claimed in claim 6, additionally comprising: (a) means for monitoring liquid temperature in the liquid storage means; and (b) means for controlling said second pump means to control the operation of said pump means responsive to the difference between the temperature monitored by the means for monitoring the temperature within the cavity and the means for monitoring the liquid temperature in the liquid storage means.

13. (Previously Presented) Apparatus as claimed in claim 1, additionally comprising means responsive to the pressure sensed by said pressure monitoring means within the cavity to control operation of said first pump means.

14 - 17. (Canceled)

18. (Previously Presented) Apparatus for modulating introduction and removal of a liquid within a cavity of a patient's body, the cavity comprising a cavity outside of blood vessels, the apparatus comprising:

a catheter configured for insertion into the cavity and introduction and removal of liquid from the cavity;

one or more sensors positionable in the patient's body so as to sense a condition of liquid in the cavity; and

a controlled pumping system operatively coupled to both the catheter and the one or more sensors, the controlled pumping system configured to control introduction and removal of liquid from the cavity so as to maintain a selected liquid condition value.

19. (Previously Presented) The apparatus of claim 18, the catheter comprising a first lumen for introducing liquid into the cavity and a second lumen for removing fluid from the cavity.

20. (Previously Presented) The apparatus of claim 18, wherein the one or more sensors are positioned on the catheter.

21. (Previously Presented) The apparatus of claim 18, wherein the one or more sensors are positioned separate from the catheter and positionable at a location separate from the catheter.

22. (Previously Presented) The apparatus of claim 18 wherein the condition is liquid pressure.

23. (Previously Presented) The apparatus of claim 18 wherein the condition is liquid temperature.

24. (Previously Presented) The apparatus of claim 18 wherein the catheter comprises a dual lumen catheter.

25. (Previously Presented) The apparatus of claim 18, further comprising a first receptacle for storing liquid to be introduced into the patient's cavity and a second receptacle for collecting liquid removed from the patient's cavity.

26. (Previously Presented) The apparatus of claim 25, wherein the first receptacle and second receptacle are coupled so as to allow recirculation of liquid.

27. (Previously Presented) The apparatus of claim 18 further comprising a second catheter configured for removal of liquid from the cavity.

28. (Previously Presented) A feedback-controlled apparatus for introduction and removal of a liquid within a cavity of a patient's body, the cavity comprising a cavity outside of blood vessels, the apparatus comprising:

a catheter configured for insertion into the cavity and introduction and removal of liquid from the cavity;

one or more sensors positionable so as to sense a biological parameter of a patient's body; and

a controlled pumping system operatively coupled to both the catheter and the one or more sensors, the controlled pumping system configured to modulate a property of the liquid in response to signals received from the one or more sensors and to maintain the biological parameter of the patient's body within a selected range.

29. (Previously Presented) The apparatus of claim 28, wherein the property of the liquid comprises rate of introduction or removal from the cavity.

30. (Previously Presented) The apparatus of claim 28, wherein the property of the liquid comprises contamination level, concentration, oxygenation, pH, or chemical agent or drug content.

31. (Previously Presented) The apparatus of claim 28 wherein the catheter comprises a dual lumen catheter.

32. (Previously Presented) A method of maintaining a liquid condition parameter within a body cavity other than a blood vessel within a patient's body, the method comprising:

pumping liquid into the cavity;

pumping liquid out of the cavity;

monitoring a parameter of liquid within the cavity from a sensor disposed within the patient's body; and

controlling at least one of liquid temperature, liquid pressure, and liquid flow rate in response to a liquid condition value measured in the monitoring step.

33. (Previously Presented) The method of claim 32 wherein the monitoring step comprises monitoring temperature of liquid within the cavity.

34. (Previously Presented) The method of claim 32 wherein the monitoring step comprises monitoring pressure of liquid within the cavity.

35. (Previously Presented) The method of claim 32 wherein the steps of pumping liquid into the cavity and pumping liquid out of the cavity comprises pumping liquids into and out of the cavity through a single catheter.

36. (Previously Presented) The method of claim 35 wherein the catheter comprises a dual lumen catheter.

37. (Previously Presented) The method of claim 32 wherein the step of pumping liquid out of the cavity comprises pumping liquid out of the cavity through an outflow catheter disposed remote from an inflow catheter through which liquid is pumped into the cavity.

IX. EVIDENCE APPENDIX

Osterholm US 4,450,841, cited by the Examiner in an Office Action dated 6/26/07.

Leonard US 3,927,980, cited by the Examiner in an Office Action dated 6/26/07.

Ginsburg et al. US 6,497,721, cited by the Examiner in an Office Action dated 6/26/07.

Gutierrez-Collazo US 5,562,821, cited by the Examiner in an Office Action dated 6/26/07.

Maginot US 6,743,218, cited by the Examiner in the Final Office Action dated 1/8/08.

X. RELATED PROCEEDINGS APPENDIX

None.

United States Patent [19]

Osterholm

[11] **4,450,841**

[45] * **May 29, 1984**

[54] **STROKE TREATMENT UTILIZING EXTRAVASCULAR CIRCULATION OF OXYGENATED SYNTHETIC NUTRIENTS TO TREAT TISSUE HYPOXIC AND ISCHEMIC DISORDERS**

[75] Inventor: **Jewell L. Osterholm**, Radnor Township, Delaware County, Pa.

[73] Assignee: **Thomas Jefferson University**, Philadelphia, Pa.

[*] Notice: The portion of the term of this patent subsequent to May 1, 2001 has been disclaimed.

[21] Appl. No.: **428,687**

[22] Filed: **Sep. 30, 1982**

Related U.S. Application Data

[60] Division of Ser. No. 354,346, Mar. 3, 1982, which is a continuation-in-part of Ser. No. 139,886, Apr. 14, 1980, Pat. No. 4,378,797, and Ser. No. 275,116, Jun. 18, 1981, Pat. No. 4,393,863, and Ser. No. 275,117, Jun. 18, 1981, each is a division of Ser. No. 139,886, Apr. 14, 1980.

[51] **Int. Cl.**[3] **A61K 31/00**; A61M 5/14

[52] **U.S. Cl.** ..... **128/632**; 604/6; 128/1 R

[58] **Field of Search** ..... 128/1 R, 630, 768, 632

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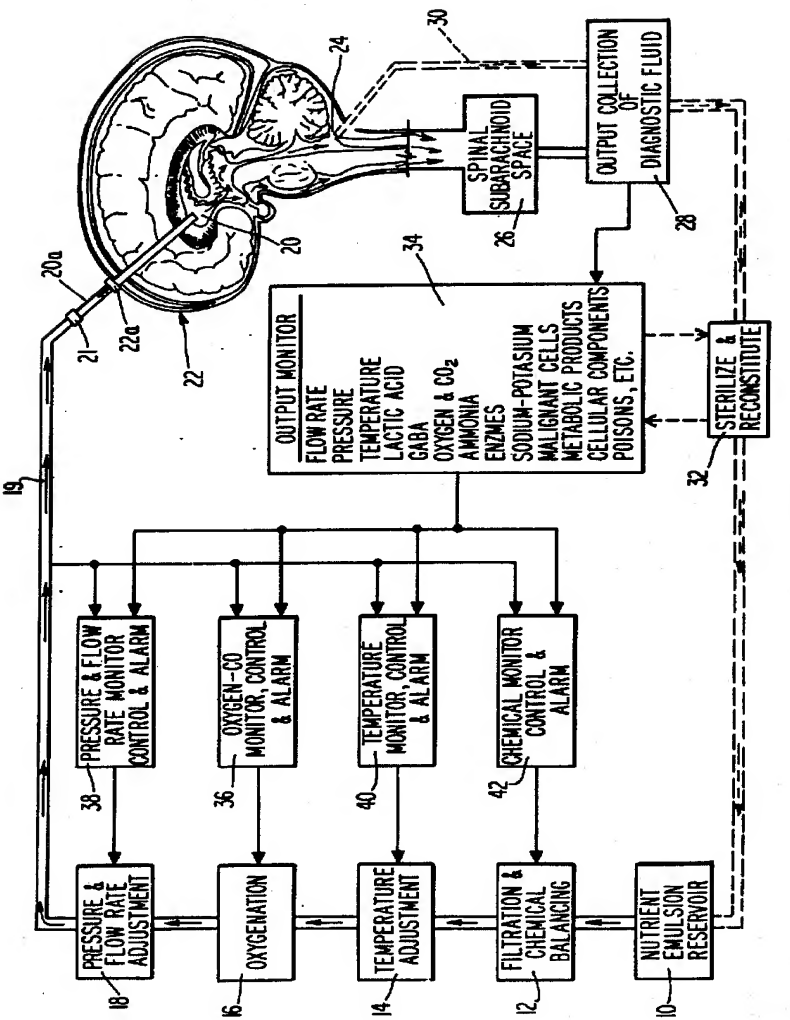
Assistant Examiner—Nancy A. B. Swisher
Attorney, Agent, or Firm—Woodcock, Washburn, Kurtz, Mackiewicz & Norris

[57] **ABSTRACT**

A novel acute care cerebral support system and method for treating severly ischemic brains is disclosed wherein an oxygenated nutrient emulsion is circulated through at least a portion of the ventriculo-subarachnoid spaces. The nutrient emulsion contains an oxygenatable non-aqueous component, an aqueous nutrient component, an emulsification component, and other components which render physiologic acceptability to the nutrient emulsion. The disclosed system and method have been shown to effectively exchange oxygen, carbon dioxide, glucose, and other metabolites in severely stroked brains. Significant restoration of oxidative metabolism and electrographic activity result from the disclosed treatment. Methods for producing the nutrient emulsion and a system for delivering that emulsion to the cerebrospinal pathway are also disclosed. Additionally, novel diagnostic methods for diagnosing the physiologic state of hypoxic-ischemic and other diseased neurologic tissue during treatment are provided.

26 Claims, 13 Drawing Figures


OUTPUT MONITOR
FLOW RATE
PRESSURE
TEMPERATURE
LACTIC ACID
GABA
OXYGEN & CO_2
AMMONIA
ENZMES
SODIUM-POTASIUM
MALIGNANT CELLS
METABOLIC PRODUCTS
CELLULAR COMPONENTS
POISONS, ETC.
SPINAL SUBARACHNOID SPACE
OUTPUT COLLECTION OF DIAGNOSTIC FLUID
STERILIZE & RECONSTITUTE
PRESSURE & FLOW RATE MONITOR CONTROL & ALARM
OXYGEN-CO MONITOR, CONTROL & ALARM
TEMPERATURE MONITOR, CONTROL & ALARM
CHEMICAL MONITOR CONTROL & ALARM
PRESSURE & FLOW RATE ADJUSTMENT
OXYGENATION
TEMPERATURE ADJUSTMENT
FILTRATION & CHEMICAL BALANCING
NUTRIENT EMULSION RESERVOIR
10
12
14
16
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20a
21
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22a
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Fig. 1

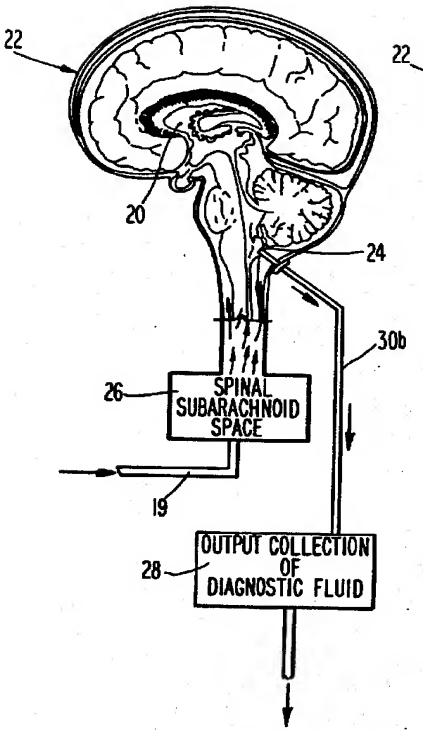
22
20
24
30b
26
SPINAL SUBARACHNOID SPACE
19
28
OUTPUT COLLECTION OF DIAGNOSTIC FLUID

Fig. 2

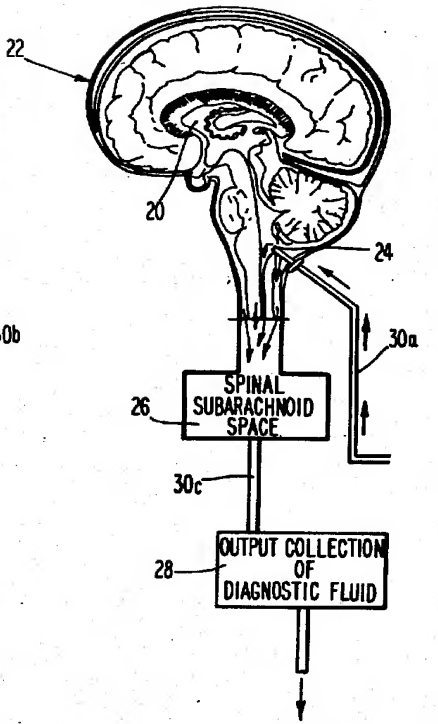
22
20
24
30a
26
SPINAL SUBARACHNOID SPACE
30c
28
OUTPUT COLLECTION OF DIAGNOSTIC FLUID

Fig. 3

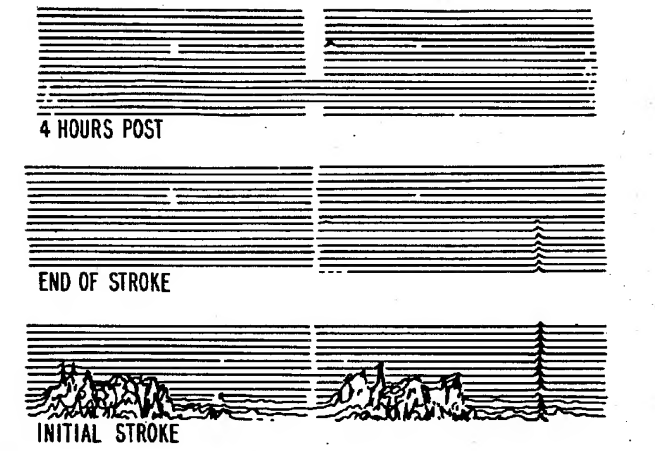
4 HOURS POST
END OF STROKE
INITIAL STROKE

Fig. 4

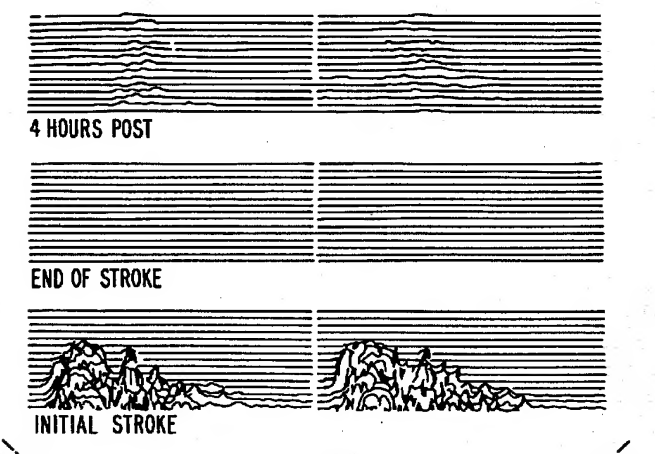
4 HOURS POST
END OF STROKE
INITIAL STROKE

Fig. 5

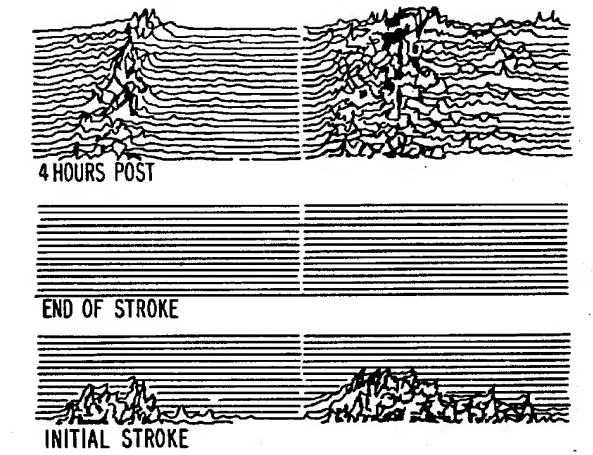

Fig. 6

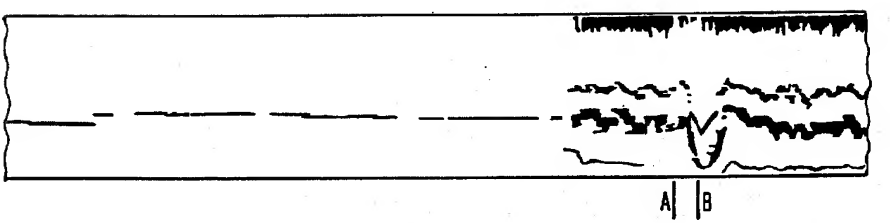

Fig. 7

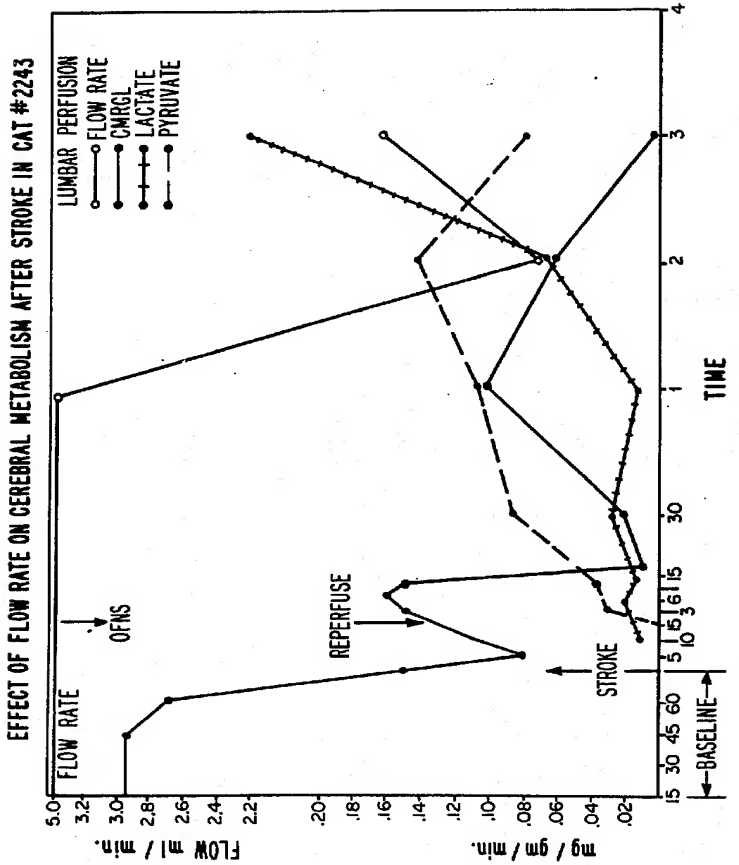
EFFECT OF FLOW RATE ON CEREBRAL METABOLISM AFTER STROKE IN CAT #2243
LUMBAR PERFUSION
FLOW RATE
CMRGL
LACTATE
PYRUVATE
FLOW RATE
OFNS
REPERFUSE
STROKE
BASELINE
TIME
FLOW ml / min.
mg / gm / min.

Fig. 8

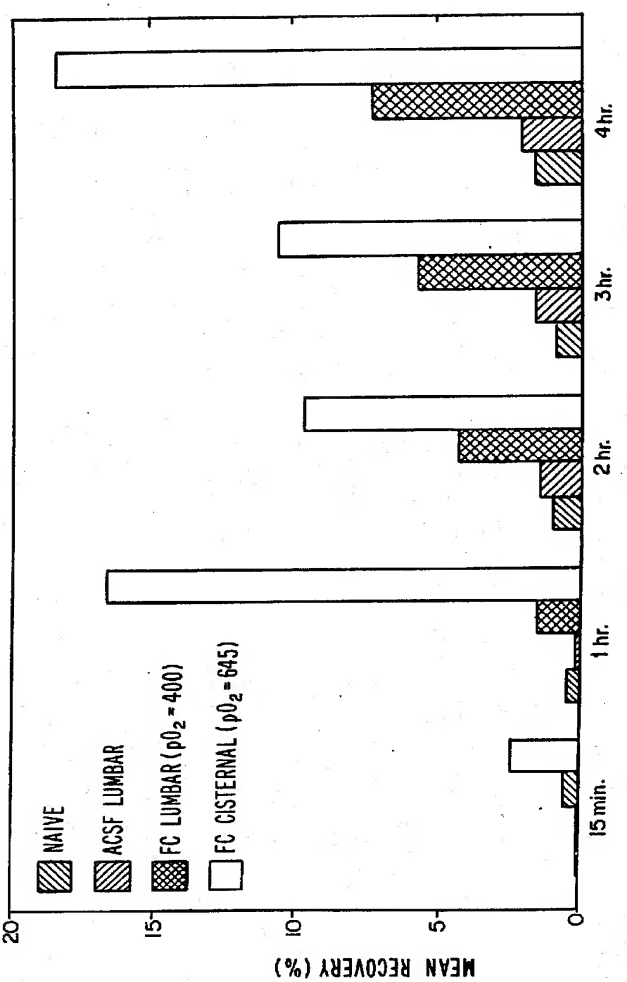
MEAN RECOVERY (%)
20
15
10
5
0
15 min.
1 hr.
2 hr.
3 hr.
4 hr.
NAIVE
ACSF LUMBAR
FC LUMBAR (pO_2 = 400)
FC CISTERNAL (pO_2 = 645)

Fig. 9

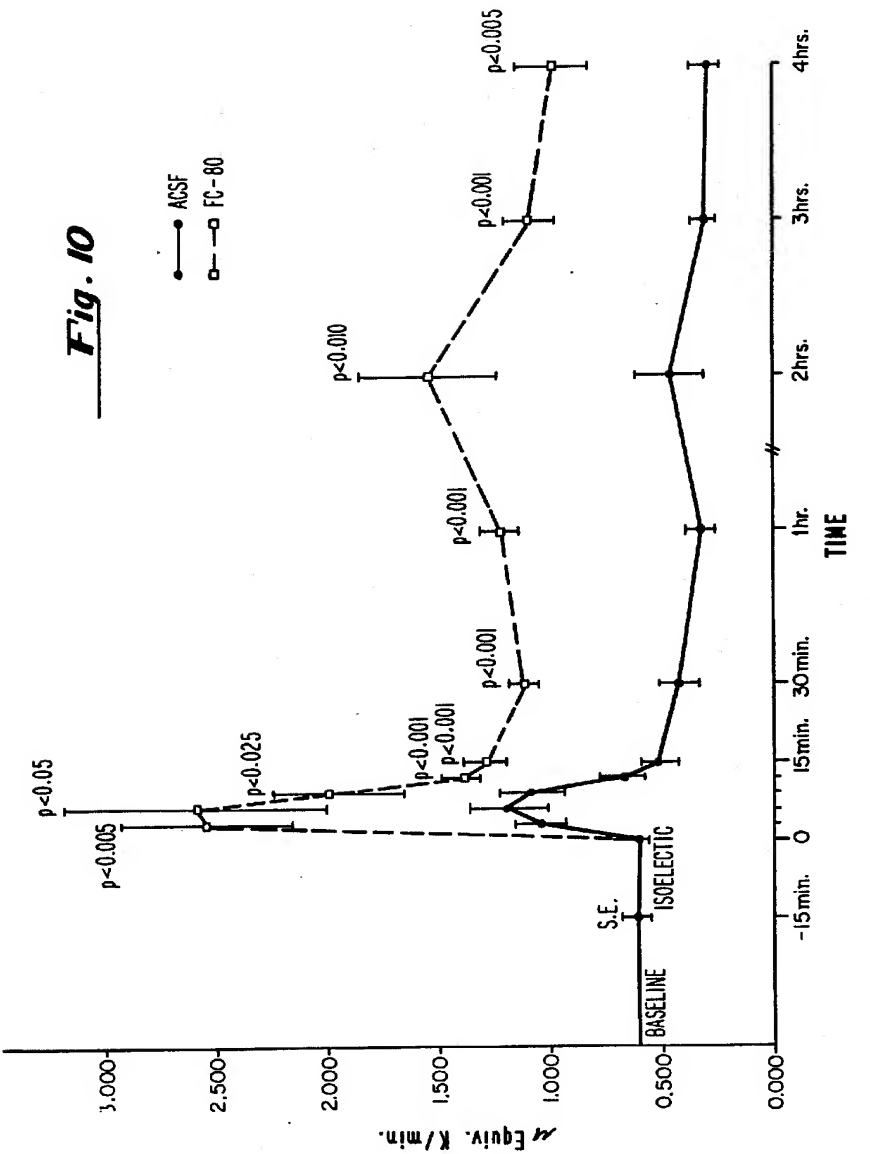
ACSF
FC-80
p<0.05
p<0.005
p<0.025
p<0.001
p<0.001
p<0.001
p<0.001
p<0.010
p<0.001
p<0.005
S.E.
ISOELECTIC
BASELINE
-15min.
0
15min.
30min.
1hr.
2hrs.
3hrs.
4hrs.
TIME
Equiv. K/min.
0.000
0.500
1.000
1.500
2.000
2.500
3.000

Fig. 10

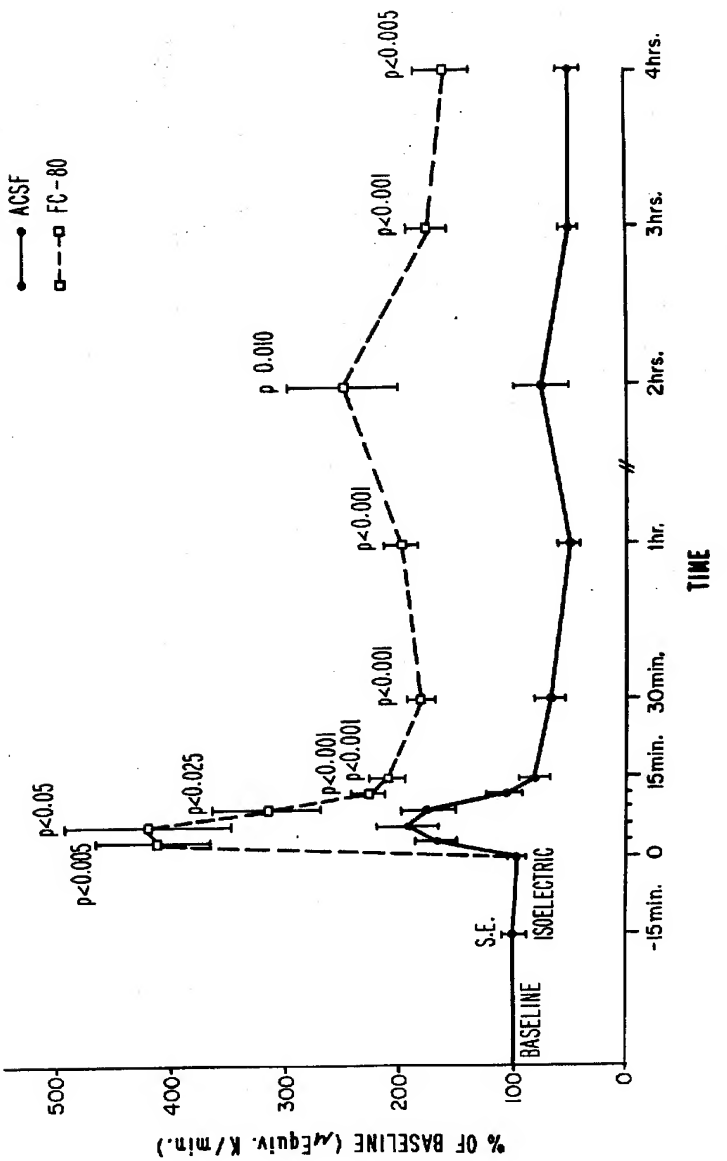
ACSF
FC-80
% OF BASELINE (μEquiv. K/min.)
500
400
300
200
100
0
BASELINE
S.E.
ISOELECTRIC
p<0.005
p<0.05
p<0.025
p<0.001
p<0.001
p<0.001
p<0.001
p 0.010
p<0.001
p<0.005
-15min.
0
15min.
30min.
1hr.
2hrs.
3hrs.
4hrs.
TIME

Fig. II

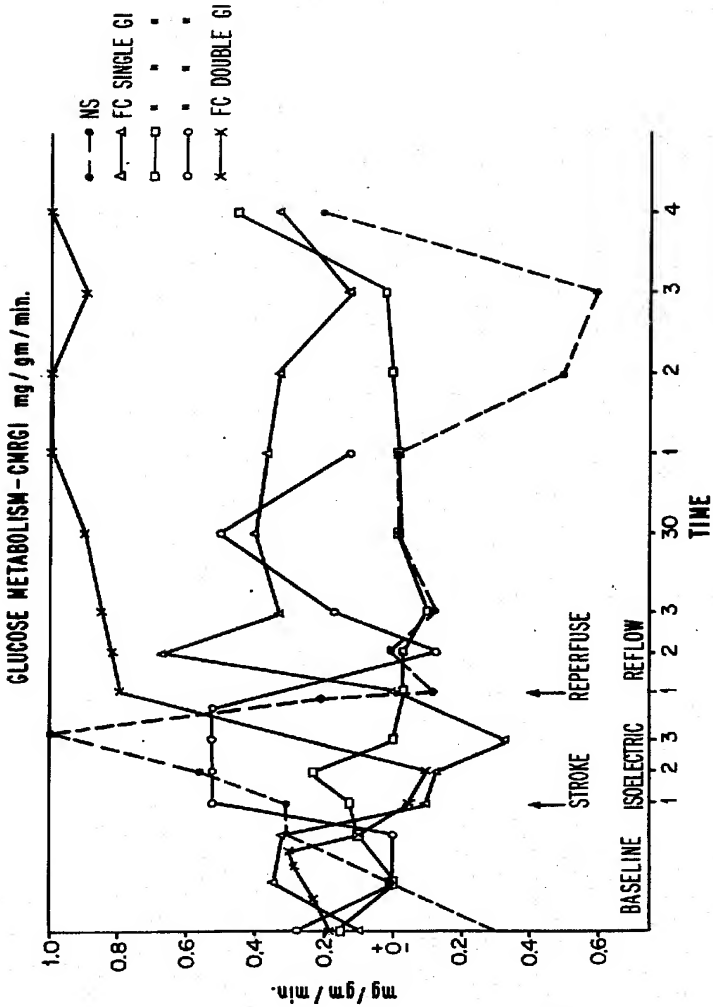
GLUCOSE METABOLISM-CMRGI mg/gm/min.
NS
FC SINGLE GI
FC DOUBLE GI
mg/gm/min.
1.0
0.8
0.6
0.4
0.2
0
0.2
0.4
0.6
BASELINE
ISOELECTRIC
REFLOW
STROKE
REPERFUSE
1 2 3 1 2 3 30 1 2 3 4
TIME

Fig. 12

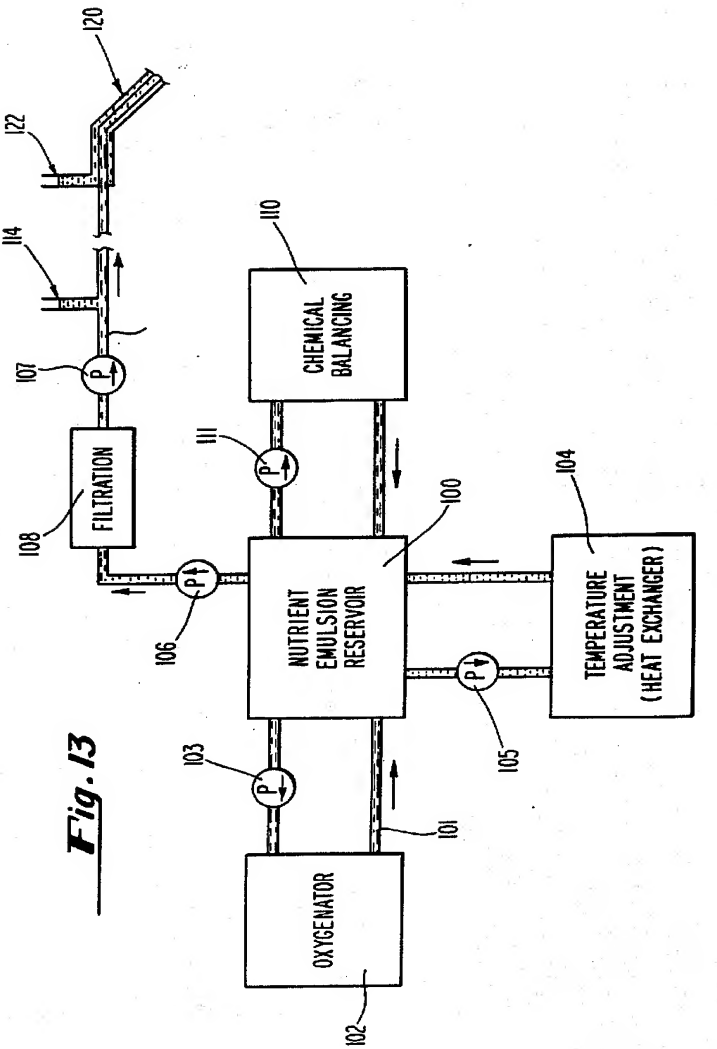
120
122
114
107
P
FILTRATION
108
110
CHEMICAL BALANCING
111
P
100
NUTRIENT EMULSION RESERVOIR
106
P
104
TEMPERATURE ADJUSTMENT (HEAT EXCHANGER)
105
P
103
P
101
OXYGENATOR
102

Fig. 13

STROKE TREATMENT UTILIZING EXTRAVASCULAR CIRCULATION OF OXYGENATED SYNTHETIC NUTRIENTS TO TREAT TISSUE HYPOXIC AND ISCHEMIC DISORDERS

CROSS REFERENCE TO RELATED APPLICATIONS

The present application is a continuation-in-part of U.S. patent application Ser. No. 139,886, filed Apr. 14, 1980, now U.S. Pat. No. 4,378,797, entitled "Extravascular Circulation Oxygenated Synthetic Nutrients to Treat Tissue Hypoxic and Ischemic Disorders", as well as Ser. No. 275,116, filed June 18, 1981, now U.S. Pat. No. 4,393,863 and Ser. No. 275,117, also filed June 18, 1981, which are in turn divisionals of Ser. No. 139,886.

BACKGROUND OF THE INVENTION

Cerebrovascular accident, a disease commonly known as "stroke", remains the third leading cause of death, and probably constitutes the single largest category of long term disability in this country. In spite of current medical knowledge and available treatments, a major central nervous system vascular occlusion is quickly attended by irreversible damage to the affected brain region(s). A "completed stroke" is manifest by a fixed and permanent neurological deficit. Millions of dollars have been expended in stroke research and care by Federal and private agencies without a single substantial gain in our present chemotherapeutic abilities for a completed stroke.

On a clinical level, once vascular flow in any portion of the central nervous system has ceased for longer than a few minutes, a permanent "stroke" invariably follows. It is not currently possible to recover substantial neural function with clinical ischemia of 5–7 minutes duration. An exquisite neuronal sensitivity to oxygen deprivation has been blamed for this ultra-short stroke irreversibility. Neurons do indeed have meager metabolic storage and are unable to meet energy needs by anerobic means. Well accepted concepts hold that such permissible cerebral ischemia times are critical and neurons must quickly be resupplied or metabolic infarction will result. While clinically true, recent laboratory investigations have addressed the problems of ischemic vascular and neuronal reactions separately with considerably different results. Recently reported studies indicate neurons are not as sensitive as previously believed. Indeed, it has been suggested that neurons can withstand global ischemia for 1 hour or longer. K. A. Hossman, P. Kleihues, *Arch. Neurol.* 29, 375–389 (1973). If the clinical and experimental observations are to be reconciled, one hypothesis is that long-term damage results from vascular rather than neuronal sensitivity to oxygen deprivation. It is known that secondary reactive changes appear within the microcirculation after sufficient stagnation. A. Ames III, R. L. Wright, M. Kowada, J. M. Thurston, G. Majno, *Am. J. Pathol.* 52, 437–448, (1968). J. Ching, M. Kowada, A. Ames III, *Am. J. Pathol.* 52, 455–476 (1968). E. G. Fischer, *Arch Neurol.* 29, 361–366, (1973). E. G. Fischer, A. Ames III, E. T. Hedly-Whyte, S. O'Gorman, *Stroke* 8, 36–39, (1977). Even if blood is represented to the local tree, the small vessels do not completely reopen. Under these circumstances ischemic, though potentially recoverable, neurons may be lethalized because they are not adequately resupplied with blood within their metabolically tolerable limits. This concept shifts the basic fault in stroke from "ultrasensitive" neurons to a protracted blood flood failure. Nonetheless, a long felt need exists to prevent permanent damage and/or reverse neurologic deficits resulting from interrupted vascular flow.

One experimental approach which has been used to investigate the effects of stroke on neurologic tissue is the perfusion of fluids of known composition through ventriculocisternal spaces. For example, E. Fritschka, J. L. Ferguson and J.J. Spitzer have reported increases in free fatty acid turnover in cerebral spinal fluid during hypotension in dogs. According to the Fritschka technique, a "mock" cerebral spinal fluid containing radiolabelled palmitate was perfused from the lateral ventricle to the cisterna magna of conscious dogs. Arteriovenous glucose and fatty acid concentrations, and "mock" CSF fatty acid concentrations were monitored over a period of 6 hours of perfusion. Estimates of the amount of palmitate recovered from the cisternal effluent and cerebral venous blood lead to the conclusion that a sizeable fraction of free fatty acids may be taken up by tissues "in the vicinity of the CSF space". See Fritschka et al, "Increased Free Fatty Acid Turnover in CSF During Hypotension in Dogs", *American Journal of Physiology*, 232:H802–H807. In "Bulk Flow and Diffusion in the Cerebral Spinal Fluid System of the Goat", by Heise, Held, and Pappenheimer, a ventriculo cisternal perfusion method was used on chronically prepared, unanaesthized goats. Measurements were made of steady-state rates at which inulin, fructose, creatinine, urea, potassium, sodium, and labelled water were removed from perfusion fluid at various hydrostatic and osmotic pressures. The subject perfusions were carried out on female goats provided with implanted ventricular and cisternal guide tubes or cannulas. Each clearance period involved perfusion of 70–120 mills of fluid through the ventricular cisternal system. Inflow rate was maintained constant in the range of 1.50–2.00 ml-min, and outflow was measured continuously. The data obtained was used to investigate the effects of hydrostatic pressure on inulin clearance, rate of formation of CSF, and the permeability of the ventricular system, particularly as compared with that of the toad bladder. This ventriculo cisternal perfusion method was first reported by Pappenheimer, Heise, Jordan and Downer in "Perfusion of the Cerebral Ventricular in Unanaestheized Goats", *American Journal of Physiology*, Vol. 203, pp. 763–774 (1962). Pappenheimer et al reported that goats are anatomically and tempermentally suited for ventricular cisternal perfusions and can tolerate such perfusions for many hours without showing signs of discomfort. The volume of the ventricular system and rate of production of CSF are at least double corresponding values reported for large dogs, and the thickness of the goat occipital bone and its shape facilitates retrograde placement of cannulas through the occipital bone into or above the cisterna magna without interfering with muscles in the neck. The goat's horns provide natural mechanical protection for the cannulas and "are almost indispensable" for operative procedures. In accordance with the Pappenheimer et al technique, guide tubes are implanted just above the dura over the cisterna magna and just above the ependymal linings of the lateral ventricules. Prior to each perfusion the cisterna and ventricle are punctured with sharp probe needles extending a few millimeters beyond the tips of the guide tubes. Alternatively, cannulas were implanted in the

subarachnoid space over the parietal cortex, thus permitting perfusion of the entire ventriculo cisternal-subarachnoid system. Pappenheimer et al followed detailed protocols for implanting the guide tubes, and for preparing sterile, synethetic CSF. The Pappenheimer et al perfusion circuit is reported to comprise a bottle sealed with a rubber cap having two stainless steel tubes extending to the bottom of the bottle. One tube serves as a gas bubbler, the second as a liquid outlet. A third opening connects with atmosphere through a sterile cotton plug. The bottle is mounted on an indicating balance and the reservoir outflow is connected through tubing to a parastalic pump with a variable drive permitting pumping rates in the range of 0.5–5 ml/min. One pump output is lead to a male syringe joint which fits the ventricular probe needles and a second outlet on the joints connects to a strain gauge manometer. A 5 ml empty sterile syringe is placed in parallel with the output to damp pulsations of the pump. The cisternal outflow is connected to an enclosed drop counter and wing flask and the output is recorded cumulatively on a polygraph which also gives a vertical record proportional to outflow rate. Pappenheimer et al reports that perfusion with CSF of normal composition can usually be maintained for 4–8 hours before the animal becomes resistive, and if correctly performed, the animal will show no sign of knowing when the perfusion pump is on or off. No attempt is made to regulate the temperature of fluid entering the ventricular probe, however at flow rates of 1–2 ml/min it is theorized that the fluid reaches temperature equilibrium with the brain before reaching the hypothalmus. At higher flow rates (4–6 ml/min) the animals are reported to start to shiver. In this regard, see also F. H. Sklar and D. M. Long, *Neurosurgery* 1, 48–56 (1977).

Over the years, many experiments have been conducted with materials possessing high oxygen-dissolving properties, many of which have been incorporated as constituents in "artificial blood". The concept of utilizing materials possessing high oxygen-dissolving properties for the maintenance of tissue respiration was first reported by Rodnight in 1954. See Rodnight, R., *Biochemistry Journal,* Vol. 57, p. 661. Rodnight capitalized upon the considerable oxygen solubility found in silicone oils, and sustained tissue slices by incubation in these oxygen laden oils. Approximately 12 years later, Clark reported experiments involving the total immersion of small animals in silicone oils and fluorocarbon liquids. Rats totally immersed in oxygenated silicone oil survived for one hour with no apparent ill effects, but died several hours after removal, from unknown causes. Similar experiments using synthetic fluorocarbon liquids, which dissolve about 3 times more oxygen than do the silicone oils, were performed with some success. Under these conditions animals survived immersion in oxygenated synthetic fluorocarbon liquids and thereafter returned to apparent health. See Clark, L. C. Jr. and Gollon F., *Science,* Vol. 152, p. 1755, (1966); and Gollon, F., Clark, L. C. Jr., *Alabama Journal of Medical Science,* Vol. 4, p. 336, (1967). While arterial oxygenation was reported as excellent for Clark's studies in rats, coincident impairment of carbon dioxide elimination was also reported, as was pulmonary damage from breathing fluorocarbon liquids. One rat, which was observed for five days following liquid breathing, was described as being in respiratory distress and as succumbing within 15 minutes after the subcutaneous administration of hydrocortisone (50 mg), with copious loss of body fluid from the trachea. In this regard, Clark concluded:

> These organic liquids should prove to be of value in studies of gas exchange in living tissues in animals. Organic liquids, since they can support respiration with oxygen at atmospheric pressure and have other unique qualities, may find use in submarine escape, undersea oxygen support facilities, and medical application. The pulmonary damage caused by the breathing of the organic liquids available at the present time remains a major complication of their use in man. *Science,* Vol. 152., p. 1756.

See also K. K. Tremper, R. Lapin and E. Levine, *Critical Care Medicine* 8:738 (1980); S. A. Gould, A. L. Rosen, L. R. Sehgal, *Fed. Proc.* 40:2038 (1981).

Following these observations, fluorocarbon liquids were used as an incubation medium for isolated rat hearts. See Gollon and Clark, *The Physiologist,* Vol. 9, p. 191, (1966). In this work, myocardial oxygen requirements were apparently well met, however these hearts did not flourish without intermittent fluorocarbon removal and washing with oxygenated, diluted blood. This phenomenon has been explained in terms of aqueous phase lack in pure fluorocarbons such that necessary ionic exchange is impeded.

More recently, considerable attention has been directed to the use of fluorocarbons as constituents of artificial blood. Sloviter, in order to overcome the problem of aqueous-metabolite fluorocarbon insolubility, made an emulsion with fluorocarbon and albumin. Sloviter's emulsion sustained the isolated rat brain by a vascular perfusion as well as did an erythrocyte suspension. See Sloviter, H. A. and Kamimoto T., *Nature* (London), Vol. 216, p. 458 (1967). A better emulsion was later developed comprising a detergent, "Pluronic F 68" (manufactured by the Wyandotte Chemical Corp., Wyandotte, Mich.), and fluorocarbon liquids which were properly emulsified using sonic energy. This improved emulsion permitted the replacement of most of the blood of a rat which was then reported as surviving in an atmosphere of oxygen for five to six hours. See Geyer "Survival of Rats Totally Perfused with a Fluorocarbon-Detergent Preparation", *Organ Perfusion and Preservation,* edited by V. C. Normen, N.Y.: Appelton-Century-Crofts, pp. 85–96 (1968), Geyer, R. P., *Federation Proceedings,* Vol. 29, No. 5, September–October, 1970; and Geyer, R. P. *Med u Ernohn,* Vol. 11, p. 256 (1970).

Experiments have also been reported wherein fluorocarbons have been used to perfuse livers. Ten hours after in vitro fluorocarbon perfusion, the isolated liver ATP; AMP; lactate/pyruvate ratio; and a number of other metabolites were found to be as good or better than livers perfused in vitro with whole blood. See Krone W., Huttner, W. B., Kampf S. C. et al., *Biochemika et Biophysica Acta,* Vol. 372, pp. 55–71 (1974). These detailed metabolic studies indicated that the organs perfused with 100% fluorocarbon liquid were redeemed "intact"; while only 75% of the whole blood infused organs maintained a similar degree of metabolic integrity. The ability of fluorocarbon perfusion to maintain cellular integrity was confirmed by electron-microscopy studies. The cells had normal mitochondrial ultra structure after ten hours of fluorocarbon support, indicating the persistence of normal or adequate aerobic metabolism. In Brown and Hardison, "Fluorocarbon Sonicated as a Substitute for Ery-

thocytes in Rat Liver Perfusion", *Surgery* 71, pp. 388–394 (1972) a fluorocarbon perfusate preserved organ function and integrity far better than perfusate with much lower oxygen carrying capacity, but was reported as resulting in a decreased rate of bile secretion which was probably the earliest sign of hepatic damage, tissue edema, and a reproducible rise of portal pressure over a period of 2½ to 3 hours. Both tissue edema and rising portal pressure with fluorocarbon perfusion were associated with progressive vascular occlusion as determined histogolically. A greatly diminished perfusion of fluorocarbon at the end of experiments was documented by injection of India ink twenty minutes before the end of the perfusion. Brown and Hardison hypothesized that the fluorocarbon perfusate may react with amino acids and proteins, that the oxygen concentration in the fluorocarbon perfusate may affect the perfusion results, and that filtration of the fluorocarbon emulsion through filter paper and differing instrumentation were responsible for the apparently conflicting results in the literature. Brown and Hardison hypothesize that phagocytosis of fluorocarbon particles might completely block reticticuloendotheilial cells in liver or that capillary endotheilial damage may be another reason for late fluorocarbon perfusion problems.

Fluorocarbons have also been used in experiments involving cerebral blood circulation. In Rosenblum's studies, mouse hematocrits were reduced to 10–15 by exchanging the animal's blood with a fluorocarbon solution. When the animals were respired with 100% oxygen after intravascular fluorocarbon infusions, the brains remained metabolically sound. These organs were able to reverse rising NADH levels and EEG abnormalities induced by short period nitrogen inhalation. The EEG's of fluorocarbon treated animals could be activated by the central nervous system stimulant metrazole. By these criteria, intravascular fluorocarbon does support the cerebral microcirculation and provides functions of oxygenation, metabolism and electrical activity which are normally associated with blood transport. Please refer to Rosenblum, W. I., "Fluorocarbon Emulsions and Cerebral Microcirculation", *Federation Proceedings*, Vol. 34, No. 6, p. 1493 (May 1975). See also S. J. Peerless, R. Ishikawa, I. G. Hunter, and M. J. Peerless, *Stroke* 12, pp. 558–563 (1981); B. Dirk, J. Creiglstein, H. H. Lind, H. Reiger, H. Schultz, *J. of Pharm. Method* 4, pp. 95–108 (1980); J. Suzuki, T. Y. Oshomoto, S. Tanaka, K. Moizoi, S. Kagawa, *Current Topics* 9, pp. 465–470 (1981).

As reported by Kontos et al, the marked vasodilation of small cerebral surface arteries which occurs in response to acute profound hypoxemia may be locally obviated by perfusing oxygen equilibrated fluorocarbon into the space under the cranial window. See Kontos, H. A., et al, "Role of Tissue Hypoxemia in Local Regulation of Cerebral Microcirculation", *American Journal of Physiology*, Vol. 363, pp. 582–591 (1978). Kontos et al described the effect of perfusions with fluorocarbon with 100% oxygen as resulting from increased supplies of oxygen to the neural cells and consequent partial or complete relief of hypoxia, rather than to a local increase in the oxygen tension in the immediate environment of the vascular smooth muscle of the pial arterioles. Two other potential explanations for the observed action are also suggested in the Kontos et al article.

In 1977, Doss, Kaufman and Bicher reported an experiment wherein a fluorocarbon emulsion was used to partially replace cerebrospinal fluid, with the intention of evaluating its protective effect against acute anoxia. Doss et al, *Microvascular Research* 13, pp. 253–260 (1977). According to this experiment, systemic hypoxia was produced through one minute of 100% nitrogen inhalation. A bolus of oxygenated fluorocarbon placed in the cisterna magna immediately prior to nitrogen breathing increased regional cerebrospinal fluid O_2 tension by a factor of 5. During the one minute experimental period, the fluorocarbon emulsion provided twice as much brain tissue oxygen as was found in saline injected controls. Doss et al found the anticipated regional tissue oxygenation decline attending nitrogen inhalation to be halved by the administration of the oxygen bearing fluorocarbon emulsion.

In spite of the above described experiments, there is yet to be reported any practical therapeutic approach to the treatment of ischemic neurologic tissue, and particularly human ischemic central nervous system tissue resulting from stroke, accident or disease.

SUMMARY OF THE INVENTION

The present invention provides a novel nutrient formulation for circulation through cerebrospinal fluid pathways, and systems and methods for using same, to treat central nervous tissue hypoxic-ischemic conditions. Through its use, a new diagnostic methodology is also disclosed.

Applicant has recognized that there is a therapeutic time window through which neuron can be reached and resuscitated. The method of the present invention is designed to bypass obstructed vascular circulation and deliver cerebral metabolic needs through an alternate cerebral spinal fluid (CSF) circulation portal. Since particle size exerts a major influence on brain penetration from CSF, the method of the present invention is hypothesized to permit diffusion of oxygen, glucose, electrolytes and essential amino acids into ischemic neural tissue when presented in abundance in the cerebral spinal pathway. Thus, a rapidly exchanging cerebral spinal fluid perfusion system is provided to amply supply these materials and, at the same time, remove metabolic waste.

The cerebrospinal fluid (CSF) pathway system, which intimately bathes and permeates brain and spinal cord tissues, constitutes a unique anatomical relationship within the body. Although it has some similarities to systemic lymphatics, its anatomical arrangement differs considerably from that of lymph. Indeed, this system has been named the "third circulation". Due to the extensive area of CSF-tissue contact over the cerebral and cord surfaces, in the miniature Virchow-Robins spaces, and cerebral ventricles, the cerebrospinal fluid system constitutes a vast, complex and intimate therapeutic avenue for access to central nervous tissue. Excepting certain infections and neoplasms where the cerebrospinal fluid is now utilized as a treatment conduit, the cerebrospinal fluid system has not been otherwise widely exploited as an easily accessible therapeutic route and has never been used as a continuous therapeutic diagnostic circulation system in man. The present invention is predicated on the recognition that, when regional cerebral blood flow is interrupted, such as after major stroke, or is otherwise seriously impeded by profound vaso-spastic states, the cerebrospinal fluid pathway actually represents the only practical and viable anatomical route by which these tissues may be readily treated. This results from the fact that the usual vascular delivery system is either occluded or non-functional,

and thus tissues within affected territories cannot be properly served.

In accordance with the present invention, essential cellular substrates are delivered to beleaguered ischemic brain regions by utilizing the "back door" cerebrospinal fluid delivery route. Accordingly, the present invention provides a novel nutrient emulsion, circulatory method and system which provide necessary nutrient penetration into regions suffering vascular deprivation.

It has been found that the cerebrospinal fluid to brain relationship is not characterized by the rigid and highly selective barrier mechanism which are present at the blood-brain interface. Thus, the penetration rate of materials from cerebrospinal fluid regions to the brain relate largely to molecular size, that is, small substances penetrate deeply while large molecules move more slowly into brain substance. Although entry rates are generally inversely proportional to molecular weight, penetration is also influenced by lipid solubility and the molecular configuration of the penetrating substance. Accordingly, the present invention provides a nutrient emulsion containing essential brain nutrients including selected electrolytes, having a relatively low molecular size which, in accordance with the methods of the present invention, are caused to relatively freely diffuse from either the ventricular or subarachnoid fluid regions into the brain matter to be treated. Accordingly, the present invention provides a novel nutrient emulsion which has been purified, balanced, and perfected to fall within narrow physiologic limits while nonetheless providing the desired nutritional characteristics referred to above.

In accordance with the preferred embodiment of the present invention, this nutrient emulsion constitutes "synthetic cerebrospinal fluid" comprising preselected electrolytes, glucose, amino acids, at least one oxygen-carrying component, typically a fluorocarbon, and other components which impart to the composition a preselected pH, buffering capability, and osmolarity. This nutrient emulsion is prepared by controlling sonication time and by properly dialyzing the materials to achieve a toxic free emulsion. The resulting solution may be rapidly oxydated to O_2 pressures of 650 mm of mercury by using the herein disclosed modified recirculating pediatric oxygenator. As a result, a novel oxygenated nutrient emulsion is provided which is believed to exhibit exceptional therapeutic properties.

The present invention also provides a novel method and apparatus for circulating the oxygenated nutrient emulsion through cerebrospinal fluid pathways, particularly those pathways which contact brain and spinal cord tissue. According to these methods, treated tissues exhibit a substantially improved ability to resist and/or repair damage which would otherwise result from vascular occlusion. In accordance with the preferred method of the present invention, the novel oxygenated nutrient emulsion is circulated through this cerebrospinal fluid route by injecting it into brain ventricles and withdrawing it from the cisterna magna or the spinal subarachnoid space to nourish and to treat central nervous tissues. In other instances the fluid may be injected into the subarachnoid space and withdrawn from another subarachnoid position. The preferred embodiment oxygenated nutrient emulsion should be circulated to tissues to be treated in amounts sufficient to provide adequate gas exchange. Pure fluorocarbon may contain 50 ml O_2 per 100 ml at one atmosphere oxygen while normal blood contains only 20 ml O_2/100 ml under the same conditions. The oxygen carrying capability per ml of the final emulsion is considerably less than that of pure fluorocarbon by reason of its content of other constituents for normalizing osmotic pressure, buffering, electrolytes, and other physiologic balancing materials. Thus, the preferred embodiment nutrient emulsion may be charged with oxygen (100% O_2 at one atmosphere) to attain pO_2 tensions of 640–700 mm of mercury and an O_2 content of 20 ml per 100 ml. Under rapid circulation conditions, the integral O_2 exchange (fluorocarbon to tissue) has been found to be about 33%. Thus, an oxygen exchange value of about 6.6 ml O_2/100 ml nutrient emulsion per minute is provided by the present method.

In accordance with the preferred embodiment of the present invention, sufficient nutrient emulsion should be supplied to counteract oxygen deprivation to the affected tissue. For example, the entire supertentorial adult cat brain weighs 12 grams (±2) and the normal metabolic consumption of oxygen of mammalian brain tissue equals 3–4 ml per 100 grams per minute. This total metabolic need may be met with the circulation rate of 6–8 mls per minute. Metabolic needs necessary to simply sustain and/or salvage tissue may be achieved by perfusion rates of one half or less of this optimum. Within these constraints an easily achieved sustenance flow rate of at least 20–30 ml/minute, optimally 45–60 ml/minute, would be anticipated to salvage 100 gms of human brain tissue. It has been found experimentally that it is possible to supply sufficient oxygen to counteract the deprivation of the affected tissue through circulation of the nutrient emulsion through the cerebrospinal fluid route. In fact, under carefully controlled conditions, it is believed within the scope of the present invention to nourish the entire human brain using the preferred embodiment apparatus, method and substance of the present invention. In this manner, central nervous neurons deprived of major blood supply may be sustained without significant damage.

In accordance with the preferred embodiment of the present invention, a novel system is disclosed for administering and maintaining the oxygenated nutrient emulsion for delivery and circulation through the cerebrospinal route.

The preferred embodiment system of the present invention effectively carries out the circulation and equilibration of the nutrient emulsion during treatment. This system, which is diagrammatically illustrated in FIG. 1, generally comprises a reservoir containing nutrient emulsion; means for delivering the nutrient emulsion at preselected flow rates; an oxygenation means for equilibrating the nutrient emulsion to desired gaseous tension levels; heat exchanger and/or cooling unit means for selectively controlling the temperature of the nutrient emulsion; filtering means for cleansing the nutrient emulsion; and circulation monitoring means for insuring that desired circulation flows and pressures are maintained within the system.

The present invention also provides a method of diagnosing conditions of neurologic tissue in mammals. This novel method generally comprises providing an artificial spinal fluid of known composition, injecting that artificial spinal fluid into at least a first portion of the cerebrospinal pathway of a mammal, withdrawing a diagnostic fluid from a second portion of that pathway to create a circulation of fluid at least through a portion of said pathway, monitoring the composition of said

diagnostic fluid, and comparing for at least a selected difference in the compositions of said artificial spinal and diagnostic fluids, whereby the detected differences in those compositions are at least diagnostic of neurologic tissue disposed along said portion of the cerebrospinal pathway. In accordance with the diagnostic methods of the present invention, the diagnostic fluids may be monitored for differences in oxygen content, lactic acid concentration, carbon dioxide concentration, potassium and/or sodium ion concentration, enzyme concentration, pH difference, ammonium concentrations, GABA (gamma-aminobutyric acid) and other amino acid(s) concentrations, microorganism content, bacterial count, myelin fragments, cellular fragments or organelles, malignant cells, and/or poisons.

It is also within the scope of the present invention to provide a novel nutrient liquid and/or diagnostic liquid for treating cerebrospinal tissue containing various novel specified components which is formulated using novel methodology.

It is additionally within the scope of the present invention to provide a novel apparatus for treating patients having ischemic-hypoxic tissues, including novel injection and withdrawal means comprising a novel catheter means which is particularly adapted for injecting oxygenated nutrient liquid into a cerebral ventricle without danger of substantially damaging neurologic tissue in the vicinity of that ventricle.

In addition to the methods described above, it is within the scope of the present invention to provide additional therapeutic agents to the nutrient emulsion, such as antineoplastic agents; antibiotics, and/or other therapeutic agents for use in treating the target tissue(s).

Accordingly, the primary object of the present is the provision of a method, substance, and system for providing early stroke treatment.

Other objects of the present invention are to provide treatments for brain and spinal cord injuries, cerebral hemorrhage, cerebral vasospasm, senility, after general hypoxia and other hypoxic-ischemic related neurological disorders.

It is a further object of the present invention to provide therapeutic treatment which may sustain the life of the brain and central nervous system tissues in case of profound shock and/or temporary cardio-respiratory failure.

It is a further object of the present invention to provide life-sustaining support to the brain and/or spinal cord tissues during the conduct of neurological or cardiovascular surgery.

Other objects of the present invention are the provision of methods which may compliment treatments of central nervous system neoplasms by either external radiation and chemotherapy by providing local tissue hyperoxygenation or drugs which may enhance drug or radiation tumorocidal effects.

Further objects of the present invention include the provision of methods which are useful in treating anoxic states attending birth injury. The present method will also assist in removal of central nervous system poisons.

These and other objects of the present invention will become apparent from the following more detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a diagrammatic view of the preferred embodiment treatment system of the present invention illustrating the circulation of nutrient emulsion from a reservoir, into a cerebral ventricle, such as a lateral ventricle, through a portion of the cerebrospinal fluid pathway for output from the spinal subarachnoid space or from the cisterna magna;

FIG. 2 is a diagrammatic view of a portion of the preferred embodiment treatment system of FIG. 1 illustrating an alternate circulation route wherein oxygenated nutrient emulsion is injected into the spinal subarachnoid space and is collected from the cisterna magna;

FIG. 3 is a diagrammatic view of portion of the preferred embodiment treatment system illustrated in FIG. 1 showing an alternate circulation route wherein oxygenated nutrient emulsion is injected into the cisterna magna for passage through the spinal subarachnoid space for withdrawal from a lumbar region;

FIG. 4 is an EEG power recording from the left and right hemispheres of a cat showing traces from the time of an initial stroke, at the end of the stroke, and four hours after the stroke;

FIG. 5 is an EEG recording of an animal perfused with oxygenated nutrient emulsion having a pO_2 level of 400 and showing a 5% return of EEG at 4 hours;

FIG. 6 is an EEG similar to FIG. 1 for an animal perfused with oxygenated nutrient emulsion having a pO_2 of 645 and showing an 88% return of electrocerebral power within 4 hours;

FIG. 7 is an EEG trace showing the effect on EEG activity of a temporary cessation in oxygenated nutrient emulsion circulation;

FIG. 8 is a graph showing the effect on glucose metabolism (CMRGl), lactate and pyruvate before and after stroke of a perfused animal particularly illustrating the effect of a reduction in perfusion rate to insubstantial levels;

FIG. 9 is a bar graph showing the mean EEG recovery (percent) for groups of cats subjected to strokes resulting in 15 minutes of EEG isoelectricity, and comparing naive animals to those perfused only with artificial cerebral spinal fluid (lumbar) and oxygenated nutrient emulsion through lumbar and cisternal routes;

FIG. 10 is a graph of microequivalents of potassium per minute versus time for two experimental groups of cats subjected to 15 minutes of a stroke induced isoelectric state;

FIG. 11 is a graph similar to FIG. 10 wherein the data in FIG. 10 is represented as a percent of the base line figure;

FIG. 12 is a glucose metabolism (CMRGl) graph plotting milligrams per grams per minute against time for three perfusions using a standard glucose concentration, one perfusion using twice that glucose concentration, and a control using artificial cerebral spinal fluid without fluorocarbon;

FIG. 13 is a diagrammatic view of an alternate embodiment oxygenated nutrient emulsion delivery system for use in performing the methods of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

In the following more detailed description, numerous examples have been selected for the purposes of explanation and illustration of the preferred embodiments of the present invention. One of ordinary skill in the art will recognize that various changes may be made in the materials and methods disclosed herein without depart-

ing from the scope of the present invention, which is defined more particularly in the appended claims.

Referring now to FIG. 1, the preferred system for circulating nutrient emulsion through a cerebrospinal pathway is diagrammatically illustrated. As shown in FIG. 1, a nutrient emulsion reservoir 10 is provided for receiving and retaining nutrient emulsion, the preparation of which will be described more fully hereinafter. In accordance with the preferred system and method of the present invention, the nutrient emulsion is injected into a cerebrospinal pathway following pH adjustment and filtering, temperature adjustment, oxygenation, and adjustment of the pressure and flow rate of the nutrient input stream. In FIG. 1, these steps are illustrated diagrammatically at 12, 14, 16 and 18 respectively. Preferably, the nutrient input stream is delivered to a ventricle of the brain, and more particular to a lateral ventricle 20 of the human brain, designated generally 22. Injection of the nutrient input stream permits the oxygenated nutrient emulsion to come into contact with the subarachnoid spaces, miniature Virchow-Robins spaces, cerebral and cord surfaces, and cerebral ventricles. For the system illustrated in FIG. 1, the nutrient input stream is diagrammatically illustrated as being injected into a lateral ventricle 20. Since the lateral ventricle is in fluid communication with other portions of the cerebrospinal pathway, withdrawal of fluid from a portion of the pathway which is remote from that ventricle will create a circulation of fluid within the cerebrospinal pathway. More particularly circulation of the nutrient input stream though at least a portion of the cerebrospinal pathway may be accomplished by withdrawing fluid from the spinal subarachnoid space, diagrammatically illustrated as 26 in FIG. 1, or alternatively, from the cisterna magna 24.

It is not necessary to conduct steps 10–18 in the sequence illustrated in FIG. 1. In FIG. 13 the presently preferred apparatus for delivering oxygenated nutrient emulsion is diagrammatically illustrated. This apparatus, which may be easily constructed using a pediatric blood oxygenator such as an H-800 Pediatric Oxygenator available from The William Harvey Cardiopulmonary Division of C. R. Bard, Inc., Santa Ana, Calif. 92705, comprises a nutrient emulsion reservoir having oxygenation and temperature adjustment loops for constantly oxygenating and adjusting the temperature of the nutrient emulsion contained within the reservoir. In this manner the flow rates of nutrient emulsion provided from oxygenation by oxygenator 102 or for temperature adjustment 104 may be independently varied through adjusting the flow rate of delivery by variable speed pumps 103 or 105 to optimize the temperature and pO_2 characteristics of the oxygenated nutrient emulsion to be delivered for injection by variable speed delivery pumps 106 and 107. As normally used, pediatric blood oxygenators fail to provide a sufficient oxygen transfer rate to fluid flow rate to accommodate the emulsion of the present invention. The minimum blood flow rate of the H-800 oxygenator, for example, is 0.5 liters per minute, and the oxygen transfer rate (to blood) at this flow rate is less than about 25 ml/min. By routing the output 101 of the oxygenator to the reservoir, the oxygenator output pump 103 may operate at flow rates which easily achieve about 7 liters per minute of oxygen transfer to the fluorocarbon carbon emulsion contained in the 2000 ml reservoir. At the same time, delivery pumps 106 and 107 may provide much lower flow rates of nutrient emulsion to the animal undergoing treatment. In a similar manner, heat exchange may also be optimized. In order to maintain optimal pO_2 values, each conduit of this system should be composed of an oxygen impermeable material to prevent leakage of oxygen from the oxygenated nutrient emulsion during processing and delivery. The filtration and chemical balancing procedures followed in preparing the nutrient emulsion are not presently performed "on line", however it is anticipated that chemical balancing may be performed as a closed loop process, as illustrated in FIG. 13. Filtration 108 is performed on line under pressure from pump 106 using a millipore bacterial filter. Pump 107 establishes the final injection rate. The flow of nutrient emulsion to the chemical balancing system is adjusted using variable speed pump 111. In the embodiment of FIG. 13, pressure monitoring and control is accomplished using an open side arm 114 bearing indicia thereon which correspond to the hydraulic pressure of oxygenated nutrient emulsion within delivery line 19. The height of the side arm is adjusted so that overflow will occur when the maximum desired intracranial pressure has been obtained.

As shown in FIG. 1 the oxygenated nutrient emulsion input stream is carried through input stream conduit 19 to an injection cannula 20*a* which is coupled thereto by coupling 21. Injection cannula 20*a* is rigidly attached to skull 22 by fitting 22*a* which holds the cannula in its proper orientation to permit injection of the oxygenated nutrient emulsion into lateral ventricle 20.

If preferred, a double lumen catheter, such as catheter 120 (FIG. 13), may be utilized in place of input cannula 20*a*. One of the lumens of this catheter should be connected to a pressure monitoring means for monitoring the intracranial pressure within the lateral ventricle 20. This pressure monitoring means may comprise an open side arm, such as side arm 122 which functions similarly to side arm 114.

The preferred injection means of the present invention comprises a cerebral catheter means for insertion into a brain ventricle. This injection means comprises means for preventing a portion of the catheter located within a brain ventricle from damaging tissues surrounding the ventricle. In the preferred embodiment, an inflatable balloon tip may be provided for this purpose. The actual injection of nutrient emulsion into the brain ventricle is accomplished by providing an arrangement of outlet holes disposed as a series of slits radially spaced around the catheter tip. Both the injection means and withdrawal means also further comprise attachment means for attaching the catheter to the body in the vicinity of the injection or withdrawal sites. Thus the injection catheter may comprise a means for fixing at least a portion thereof with respect to the skull to insure catheter stability. The withdrawal catheter, which may have a tip with multiple perforations disposed therein, further comprises means for attaching at least a portion thereof to tissue in the region of the subarachnoid space. This attachment means may include a staple for attaching a non-collapsible portion of the catheter to a lumbar region of the skin.

In many applications, the oxygenated nutrient emulsion will be delivered under normothermic conditions, that is, at about 37° C. Under these conditions, and under hypothermic or hyperthermic conditions where the delivery temperature of oxygenated nutrient emulsion is higher than ambient temperature, temperature adjustment is easily accomplished by providing a thermostatically controlled heater coupled to a suitable heat

exchanger for adjusting the temperature of oxygenated nutrient emulsion recirculated to the nutrient emulsion reservoir.

The circulation route illustrated in FIG. 1 permits the treatment of at least cerebral tissues. It is within the scope of the present invention, however, to focus treatment on selected neural tissue areas, in which case alternative points of injection and withdrawal of fluid may be selected by the attending physician. For example, in the case of spinal cord injury, it is anticipated that the point of injection of oxygenated nutrient emulsion may be the lumbar, spinal subarachnoid space, with the point of withdrawal being the cisterna magna. While the above mentioned cerebrospinal pathway injection and withdrawal points are preferred, it is within the scope of the present invention to utilize other injection and withdrawal locations, provided a substantial circulation of fluid through the area of affected neurologic tissue is established by utilizing the selected loci. Such alternate pathways are illustrated in FIGS. 1–3. In FIG. 1, withdrawal of the nutrient emulsion from the cisterna magna is illustrated via conduit 30 in dotted outline. In FIG. 2 input conduit 19 injects oxygenated nutrient emulsion into the diagrammatically illustrated subarachnoid space 26. Withdrawal from the cisterna magna is via conduit 30*b*. In FIG. 3 injection into the cisterna magna is accomplished via injection catheter 30*a*. Withdrawal is from the diagrammatically illustrated spinal subarachnoid space 26 via withdrawal catheter 30*c*.

The fluid which is withdrawn from the cerebrospinal pathway will not be of identical composition to the oxygenated nutrient emulsion which is injected at the injection point. By taking advantage of differences in composition which are detected in the withdrawn fluid, which may be considered to be a diagnostic fluid, the attending physician may easily monitor the physiologic condition of the neurologic tissue which is being treated. This diagnostic fluid may also be monitored to assure that treatment is proceeding according to plan. Accordingly, fluid which is withdrawn from the cerebrospinal pathway is directed to an output collection means 28 for collecting diagnostic fluid. Preferably, an output monitor 34 will continuously monitor various chemical and physical characteristics of the diagnostic fluid for such properties as flow rate, hydraulic pressure, potassium and sodium ion concentration, temperature, lactic acid concentration, gamma amino butyric acid and other amino acid concentrations, oxygen concentration, carbon dioxide concentration, enzymes, and ammonia concentration. The output of this output monitor will not only provide the attending physician with information concerning the state of the cerebrospinal tissue being treated, but also will be fed back to the monitor, control and alarm systems for at least pressure and flow rate, temperature, oxygen-carbon dioxide and chemical constituency, as described more fully hereinafter. This diagnostic system takes advantage of the fact that ischemic neurologic tissue produces higher concentrations of such materials as Gamma-aminobutyric acid (GABA), lactate ion (lactic acid), enzymes and/or LDH (lactic dehydrogenase), ammonia, and other constituents which have been determined by analyzing cerebrospinal fluid of patients subjected by disease to similar anoxic conditions.* In accordance with the system of the present invention, however, a continuous monitoring of the state of neurologic tissue is possible, since the circulation of oxygenated nutrient emulsion will produce a continuous flushing of the affected tissue regions, and thus will result in diagnostic fluid component variations which are rapidly reflective of the physiologic state of the tissues being treated. Due to the multipoint injection-withdrawal method of the present invention, dangers which are inherent in sampling natural cerebrospinal fluid at a single location are avoided by utilizing a double venting method wherein the cerebrospinal fluid pressure is at all times carefully controlled.

*See for example, "Rapid and Sensitive Ion-Exchange Fluorimetric Measurement of G-Aminobutyric Acid in Physiological Fluids", Hare et al, *Anal. Biochem.* Vol. 101, pp. 349–355 (1980) for a preferred GABA measurement method.

It is within the scope of the present invention to sterilize and reconstitute that diagnostic fluid as shown at step 32, whereupon that reconstituted diagnostic fluid may be provided as nutrient emulsion to the nutrient emulsion reservoir 10. As shown in FIG. 1, the output monitor 34 may monitor the diagnostic fluid during the sterilization and reconstitution processes and, if desired, ensure that the reconstituted fluid satisfies the requirements of the nutrient emulsion reservoir. As shown in FIG. 1, in order to ensure that appropriate degrees of oxygenation, filtration and chemical balancing, temperature adjustment, and pressure and flow rate are maintained, the nutrient input stream is monitored by various monitors, controls, and alarms, which are intended to provide a fail-safe nutrient input stream. In particular, a pressure and flow rate monitor, control and alarm 38 is provided for monitoring the pressure and flow rate of the nutrient input stream, for controlling the pressure and flow rate adjustment 18 to establish desired pressures and flow rates, and for sounding an alarm in the event that the nutrient input stream exceeds or falls below preselected pressures or flow rates. If desired, this alarm may additionally disable the pumping mechanism producing flow of the nutrient input stream such that the unit "shuts down" upon detection of unacceptable input stream conditions.

Referring now to the temperature monitor, control and alarm, the temperature characteristics of the nutrient input stream are similarly detected, at least to ensure that hyperthermic states, except when used as therapeutic modality, are avoided. While in most instances, the nutrient input stream will be adjusted to a 37° C. temperature, it may be desired to select hypothermic temperatures in order to establish certain treatment conditions. In either event, the temperature monitor will continuously detect the temperature of the input stream, will control the temperature adjustment 14 to establish a preselected temperature, and will sound an alarm and/or disable the system in the event that a preselected temperature range is not maintained in the nutrient input stream.

Referring now to the chemical monitor, control and alarm 42, the nutrient input stream will be continuously monitored for one or more chemical or physical characteristics of the nutrient input stream, and will control the chemical balancing, filtration, etc. which is performed by the filtration and chemical balancing unit 12. The chemical monitor, control and alarm may, for example, monitor the pH, osmolarity, electrolyte component, carbohydrate component, amino acid component, or other components of the nutrient emulsion to ensure that the nutrient input stream falls within preselected stream characteristics. In the event that these characteristics do not fall within the preselected range, the alarm for unit 42 may sound and/or may disable the system to

thereby prevent further injection of nutrient input stream into the cerebrospinal pathway.

Finally, an oxygen/carbon dioxide monitor, control and alarm unit **36** is provided which continuously monitors the oxygen and carbon dioxide contents of the nutrient input stream, which controls the oxygenation unit **16**, and which sounds an alarm in the event that the oxygen or carbon dioxide concentrations do not fall within preselected ranges. It is anticipated that each of units **36–42** may provide continuous displays of the information monitored from the nutrient input stream, and may, if desired, enable back-up units which either manually or automatically supplement or replace the functions of units **12–18** in the event that those units are not functioning to produce a nutrient input stream within the desired ranges. For example, it is anticipated that a manual or battery operated pump, oxygenator, filter, and pressure and flow rate adjustments be provided to enable emergency operation of the system, since continual nutrient flow is lifesaving for the devitalized portion of the treated organ.

The preferred nutrient emulsion of the present invention is comprised of carefully formulated components which, to the extent possible while maintaining desired therapeutic activity, mimic the physical and chemical characteristics of natural cerebrospinal fluid. Generally, tissues and cells will not fair well if exposed to large volumes of non-physiologic ionic solutions. Accordingly, it has been recognized that appropriate electrolyte compositions at the tissue level are indispensable when it is considered that the circulatory method of the present invention would otherwise result in the washing and the dilution of electrolytes from the region even after short terms of circulation, to the detriment of cell membrane functions. Accordingly, in accordance with the preferred embodiment of the present invention, sodium, potassium, calcium, magnesium, and chloride ions are carefully balanced in the nutrient emulsion of the present invention to thereby create, to the degree possible, normal extra-cellular compositions. The present invention also provides a non-aqueous oxygen transfer component for selectively combining with oxygen and for transferring oxygen to the tissues to be treated. Numerous compounds are known to the art which are characterized by having a high solvent property for oxygen, carbon dioxide, and other gases. The preferred non-aqueous oxygen transfer component of the preferred nutrient liquid should exhibit when so charged, oxygen vapor pressure ranges of above 400, and preferably 600, Torr. Such oxygen transfer components should similarly not have in themselves high vapor pressures which would boil at body temperatures, nor have viscosities which are difficult if not impossible to emulsify. Generally, the preferred compounds for use as non-aqueous oxygen transfer components are fluorocarbon polymers, such as perfluorocarbons, perfluorinated alkyl polyethers, fluoroethers, fluoramines, etc. While compounds within these groups range in molecular weight from 250 to 7000, their selection for use as non-aqueous transport components are based upon the combination of features of the proper vapor pressure, molecular weight, viscosity, and emulsifiability, emulsion-stability and tissue distribution. One such fluorocarbon which has been found to be particularly suited for the non-aqueous oxygen transport component of the preferred nutrient liquid is a reagent grade perfluorobutyltetrahydrofuran which has been sold by the 3-M Corporation under the trademark "FC-80". FC-80 has an oxygen solubility coefficient ScO_2 of 0.45 of ml O_2/ml at pO_2 of 760 Torr. See Navari et al., *Res. Exp. Med.* 170, pp. 169–180 (1977), which paper is specifically incorporated by reference as if fully set forth herein. It should be noted that whole blood under the same circumstances contains 0.23 ml O_2/ml. The FC-80 ScO_2 is linear from 760 to 200 Torr but declines quite rapidly below the lower level. The high oxygen diffusion coefficient (5.71×10^{-5} cm^2/sec per second) indicates more than adequate FC-gas in a physiologic sense. Similar studies concerning CO_2 solubility and diffusion indicate that absorption and release are described by a straight line function. From these observations, metabolic tissue CO_2 accumulations should theoretically be easily removed by fluorocarbon solutions administered through a circulatory method.

Not only do fluorocarbons possess these unique physical gaseous properties but they are for the most part non-toxic. The main acute toxicity has been found to reside in free fluoride ion accumulation which occurs mainly from sonication. See, Clark et al., *Fed. Proc.* 34, pp. 1468–1477 (1979). The free ion can, however, be removed by repetitive dialysis and the emulsion thereby rendered physiologically acceptable. Accordingly, the preferred embodiment nutrient liquid of the present invention, which has been dialysized and filtered through a millipore filter, has evidenced no toxicity either in short term or long term use during circulation through cerebrospinal pathways of animals. One chief advantage of the CSF circulation route is that most or all the nutrient liquid can be removed by washing at the time of treatment termination. In this way long term cellular retention as previously noted for liver and reticuloendothelial cells in vascular circulations of oxygenating liquids may be avoided.

In the preferred embodiment nutrient liquid of the present invention, an emulsification component is provided for permitting the emulsification of the nutrient component with the oxygen transfer component of that liquid. See Clark et al, *Triangle II*, pp. 115–122 (1972b); Clark et al, *Microvasc. Res.* 8, pp. 320–340 (1974). The best currently available material for this purpose is believed to be block polymer polyols, which are known to the art as "pluronics", of which, pluronic F68 has proven to be a most efficient emulsifying agent. As used in a nutrient liquid as described more fully hereinafter, the toxicity from such a pluronic detergent is negligible. At the present time, however, it is anticipated that other emulsification components which will permit the non-aqueous transfer component of the nutrient liquid to become soluble with respect to the aqueous nutrient component of the nutrient liquid may be utilized to provide solutions which have adequate physiologic perimeters. Such other means of solubilizing fluorocarbons includes the formation of micelles, etc.

In the preparation of the preferred nutrient liquid, an important factor in producing an acceptable nutrient liquid is the achievement of an acceptable final osmotic pressure. The osmotic pressure of the nutrient liquid will depend upon the amount of the emulsification component, the particle size of the fluorocarbon, and the ionic composition of the aqueous nutrient component. In accordance with the preferred method of preparing the nutrient liquid of the present invention, toxic emulsification components should be removed by dialysis. Fluorocarbon particle size will be controlled by sonification time and filtering, while the ionic composition of the aqueous nutrient component will be carefully ad-

justed to produce a nutrient liquid possessing desired osmotic characteristics. If desired, a final osmotic tuning may be accomplished in accordance with the method of the present invention by adding ascorbic acid to the nutrient liquid.

In order to provide fully successful treatment of ischemic tissues, it is desirable to provide nutrient liquid for circulation around those tissues which will compensate for relative or complete deficiencies of blood transport metabolites. In addition to oxygen, other tissue metabolic requirements include glucose, amino acids, ions, hormones, vitamins, etc. While in temporary treatment conditions, it may be suitable to temporarily omit one or more vitamin, hormone, ion, or amino acid, for prolonged treatment and to produce the most desirable results, it is preferred to provide substantially all of the above mentioned metabolites in the preferred nutrient liquid. It is at least desirable to provide in the nutrient liquid all components necessary to support aerobic metabolism which will be available within the medium for use at cellular levels. Glucose deprivation of central nervous system tissue causes a serious cellular metabolic deficiency, as does the same degree of oxygen deficiency. Accordingly, by providing a total and finely adjusted mixture that has all the necessary components for total cell survival, an extremely efficient and therapeutic liquid material is provided which is ideal for circulation through the cerebrospinal pathways.

In order to illustrate the preferred method and composition of such an oxygen-nutrient material, the following example is provided.

EXAMPLE 1

Under conditions of replacing blood borne materials by perfusion all nutrients necessary for aerobic metabolism must be available within the medium for immediate use at cellular levels. As far as the central nervous system is concerned, glucose deprivation causes as serious a cellular metabolic deficiency as does the equivalency of oxygen lack. To achieve the desired ends all known essential nutrients have been added to the FC (fluorocarbon) emulsion. FC itself thereby serves the purpose of a gas transport system while the aqueous emulsion phase contains an array of cellular metabolic essentials. The total and finally adjusted mixture has all the necessary ingredients for total cell survival. The combination material is referred to as an oxygen-nutrient formula (Ox-N), or oxygenated nutrient emulsion.

Method and Composition Preparation of Oxygen-Nutrient Material

1. Reagents
   - (A) 5% Commercial grade Pluronic F68 (Basic Wynadotte).
   - (B) 20% W/V FC-80 (3M Corporation)
   - (C) Synthetic C.S.F.

Sodium Chloride	7.3 gm/L
Potassium Chloride	300 mg/L
Calcium Chloride (dehyd)	200 mg/L
Magnesium Sulfate	300 mg/L
Sodium Phosphate (hepta)	200 mg/L
Sodium Bicarbonate	190 mg/L

Adjust the pH to between 7.380–7.420 with 10% Ascorbic Acid

   - (D) Bacitracin Inj. 50,000 U/vial (Pharmacy) reconstitute with 10 ml saline to give a concentration of 5000 U/ml. Use 0.2 ml for each liter of perfusate to obtain a concentration of 1,000 units per liter of perfusate.
   - (E) Essential Amino Acids (Pool) (Sigma)

-continued

Method and Composition Preparation of Oxygen-Nutrient Material

D-Glutamic Acid	11.8 mg
L-Glutamine	730.0 mg
DL-Serine	26.3 mg
D-Threonine	30.0 mg
D-Lysine	38.8 mg
D-Valine (optional)	19.0 mg
D-Leucine	14.0 mg
DL-Isoleucine	13.0 mg
D-Phenylalanine	15 0 mg
DL-Tyrosine	14.0 mg
D-Methionine	4.5 mg

Before oxygenating the fluorocarbon emulsion add 9.8* mg. amino acid and 200 mg dextrose for each 100 ml of emulsion.

   - (F) Steroid (Methylprednisolone sodium succinate) 125 mgs. (The Upjohn Company). Reconstitute the steroid with 2 ml of diluent to obtain a concentration of 62.5 mg/ml. Add 0.5 ml of this mixture to each liter of emulsion before oxygenation (31.2 mg/L).
   - (G) 1 N NaOH

2. Materials
   - (A) Sonifier Cell disrupter (Branson) Model W185D
   - (B) Waring Blender for mechanical dispension of Pluronic Acid.
   - (C) Dialyzer tubing ¾ in. (22 mm) (Thomas). It is necessary to dialize the emulsion to remove fluoride ions as well as other low molecular weight contaminants.
   - (D) Whatman Filter Paper #1 (46 × 57) (Thomas) The emulsion should be filtered to remove particles originating from disrupted carbon skeletons of flurocarbon during sonication.
   - (E) 0.8 micron filter unit (Thomas). Sterilization is accomplished by filtering the emulsion through a micro filter.
   - (F) CO_2 tank (Welders Supply Company) CO_2 is used as a defoaming agent while sonicating.
   - (G) 100% O_2 tank (Welders Supply Company) CO_2 is used as a defoaming agent while sonicating.
   - (H) 100% O_2 tank (Welders Supply Company) for saturating perfusate.
   - (I) Sterile Culture Flasks (Thomas) for storing perfusate.
   - (J) Gas Dispersion Tubes (Fisher Scientific Company) for equilibrating the emulsion with O_2.
   - (K) Aspiratory Bottle (Thomas)
     a. 250 ml capacity-cut off 2¼" from the neck with a glass cutter in order to accommodate the macrotip for sonification.
     b. 500 ml capacity - for equilibration of the emulsion with 100 ml capacity - 100% O_2.
   - (L) K50 Extension tubing. Capacity approximately 2.1 ml length 40.7 centimeters (20 in.).
   - (M) Circulating Pump
   - (N) Sonification Assembly
     a. Fill a container with crushed ice; one that will allow drainage of the water as the ice melts (a fish tank will do).
     b. On the serrated outlet near the bottom of the aspiratory bottle connect seven lengths (140 in.) of K50 extension tubing. Place the bottle in the ice bath and connect the tubing to circulating pump.
     c. Place the precooled Pluronic acid in the aspirator bottle. Drape and return extension tubing from the pump over the side of the bottle. Drape the tubes from the CO_2 tank over the side of the bottle and bubble slowly. Carefully lower the macrotip into

-continued

Method and Composition Preparation of Oxygen-Nutrient Material

the solution and start sonification.

3. Method 20% FC-80 (5% Pluronic (F68)) (w/v)
   (A) Place 25 gms of F68 + 250 ml of artificial CSF in a Waring blender and blend at a high speed for 2 minutes. The solution will become very foamy. For best results the solution should be refrigerated overnight before using. This allows the head of foam to settle and precools the solution to the proper temperature for sonification.
   (B) Place the precooled Pluronic acid solution in the aspirator bottle. Turn on Sonifier. With a Pasteur pipette add 58.8 mls (100 gm) of FC-80 over a 30 minute period sonifying throughout. Once added allow the mixture to sonicate for 45 minutes. Be sure that the temperature does not exceed 20° C.
   (C) Cut dialyzer tubing that has been pre-soaked in artificial C.S.F. into 60-inch strips. Fill each strip half full with the mixture. Place strips in containers filled with approximately 1000 ml, of artificial C.S.F. Refrigerate and allow to dialize for 48 hours. The dialyzing solution should be changed every twelve hours, and the emulsion checked and transferred to additional tubing since the volume is considerably increased during dialysis.
   (D) After dialysis filter the solution through Whatman #1 filter paper, then take the total volume. 25 gm of Pluronic acid and 58 750 ml of emulsion. The former volume represents 20% FC-80 and 5% F68 w/v ratio. The emulsion should be kept in an ice bath while processing.
   (E) Add bacitracin to the emulsion. The pH at this point should be between 6.5 and 6.8.
   (F) It is necessary to adjust the electrolytes at this stage.

Unadjusted electrolytes:		
Na	=	127
K	=	5
Cl	=	126
CO_2	=	1.5
Osmolarity	=	271

It is necessary to add 696 mg NaCl/L of emulsion in order to normalize the electrolytes.

Adjusted electrolytes:		
Na	=	131
K	=	3.8
Cl	=	130
CO_2	=	3
Osmolarity	=	303

   (G) Using 1.0N NaOH adjust the pH to between 7.380 and 7.420, then check the osmolarity (Range 298–317)
   (H) Sterilize the emulsion by filtering through 0.8 micron filter. The emulsion can be frozen at −20° C. and is stable for several months.

4. Immediately Before Using Emulsion
   (A) Add: Glucose 0.8–2.5 gm/L; Amino Acid 0.098 gm/L; Steroid 31.2 mg/L (optional)
   (B) Warm the emulsion to 37° C. and equilibrate with 100% O_2 using a gas dispersion tube for 30 minutes to obtain a pO_2 of between 580–660.
   (C) A typical batch of FC-80 emulsion shows the following properties

Na	=	131 meq/L
K	=	3.8 meq/L
Cl	=	130 meq/L
CO_2	=	3 meq/L
Glucose	=	186 mg. %

-continued

Method and Composition Preparation of Oxygen-Nutrient Material

Osmolarity	=	311 mOsM

   (D) A typical batch of oxygenated nutrient emulsion contains:

Fluorocarbon	=	78.6 ml/L
Pluronic Acid	=	213 ml/L
NaCl	=	7.3 gm/L
Potassium Cl	=	300 mg/L
Calcium Cl (dehydrated)	=	200 mg/L
Mg Sulfate	=	300 mg/L
Sodium Phosphate	=	200 mg/L
Sodium Bicarbonate	=	190 mg/L
Amino Acid Pool (added to fluoro-carbon)	=	0.098 gm/L
Manitol Injection USP 259	=	50 ml/L
Bacitracin	=	5000 units/L
Gentamicin	=	80 mg/L
Dextrose	=	2 gm/L
Ascorbic Acid (10%)	=	0.5 ml/L
Sterile Water	=	remainder per liter

*Siegel et al., Basic Neurochemistry (2nd edition), Little, Brown and Company, Boston p. 297.

Gas Characteristics After Oxygen Equilibration		
	Unsaturated	Saturated
pH	7.231	7.342
pCO_2	3.7	5.7
pO_2	190	640.5

In order to provide an indication of the efficacy of the preferred treatment methods, the following examples are provided:

EXAMPLE 2

For reasons of simplicity and reproducability a model continually in use in applicant's laboratory has been employed. Osterholm, J. L., *Pathophysiology of Spinal Cord Injury*, C. C. Thomas, Springfield, Ill. (1978). Extensive experience with spinal cord injury in terms of standardization, quantitative histological studies, regional blood flow and biochemical parameters suggested these procedures. A primary pathophysiologic event in that model has been determined to be discrete regional ischemia. A microcirculatory flow failure within the injured region has been documented by many study techniques including microangiography, distribution of intravascular particulate materials, hydrogen-platinum flow studies, regional istopic techniques and lactate accumulation. Recent C 14 antipyrine microregional blood flow studies conducted in applicant's laboratory have accurately delineated the magnitude of ischemia in the injured cord. Within one hour the regional grey matter flow drops from the control of 44 cc/100 gm/min to only 2 cc/100 gm/min. The white matter is also ischemic. Blood flows in these regions are depressed from 15 cc/100 gm/min to 1–2 cc/100 gm/min.

From these observations, standarized spinal cord injury causes a restricted ischemic lesion which can be easily studied and quantitated. In this rigid system therapeutic treatment effects are readily detected by comparison with our extensive untreated injury data. It should be noted here that the mechanical injury forces used in these experiments are substantially above saturation and

all wounded animals are rendered permanently paraplegic.

Circulation Experiments

Experiments were carried out by continuously injecting either saline or Ox-N emulsion saturated with O_2 at 1 atm into the distal subarachnoid spinal space. The outflow (withdrawal) of the diagnostic fluid was at the cisterna magna. Infusions were begun immediately after severe wounding. An infusion rate of 3 ml/minute was easily achieved, and this rate was maintained for two hours.

Oxygen

Prior to lumbar spinal infusion we were able to develop pO_2 tensions of 535 ± 89 mm O_2 in the Ox-N emulsion by simply bubbling 100% oxygen through the solution. Upon exit at the cisterna magna after traversing the entire spinal subarachnoid space the pO_2 had fallen to 243 ± 63. The oxygen difference between entering and exit was 292 ± 63, or a 55% decline, which is statistically significant at the $P < 0.001$ level. This finding indicates a rapid pO_2 exchange during the thirty seconds or less transit time. For various technical reasons our initial pO_2 was lower than can be achieved under idealized circumstances. More recently it has been possible to regularly attain pO_2 of about 650 Torr. Even better experimental results might have now been obtained under conditions of higher O_2 tension.

Carbon Dioxide

FC-80 is an efficient CO_2 exchange and transport agent, and the emulsion therefore easily extracts tissue CO_2. This is indicated by an initial emulsion pCO_2 of 2.7 Torr which rose to 16.0 Torr after the tissue perfusion contact. This represents a 593% increase in FC-80 CO_2 ($P < 0.001$). The emulsion also removes other acid metabolites since in some experiments the inherent buffering capacities were exceeded as the exit fluid pH exhibited a considerable depression toward the acid side (original pH 7.4, exit pH 7.0). This pH change exceeded any acid contribution by the collected CO_2, and amounted to 0.248 mole lactate/hour.

A. Cross Sectional Area (Edema)

Frozen tissues were sectioned and stained (H & E, and acid phosphatase). The sections were evaluated by projection to 25× magnification and preselected lesion parameters measured by means of a compensating polar planimeter. There was considerable increase in the untreated injury cord cross sectional area (1280 mm^2) which was significantly reduced in the Ox-N experiments, (896 mm^2). We have assumed that this substantial cross sectional cord area increase is caused by edema fluid. In the course of other experiments, the degree of edema appearance has been quantified. It was found that net water accumulation at those post injury times ranged from 25% to 40%. The absolute reduction in cross sectional area by the Ox-N treatment is significant at the $P = 0.001$ level.

Lesion Size

Using our standard sampling methodology which includes skip serial sections throughout the injury region, and analysis by quantification techniques, the degree of injury induced hemorrhagic necrosis can be determined. With the perfected injury system the lesion size at any time point can be reliably predicted. The effects of saline and Ox-N circulations upon lesion size were compared to each other and to our established untreated values. The results are summarized in Table I:

TABLE I

	LESION SIZE 2 Hour Injuries		
	% Grey	% White	% Total
Standard Injury (No Infusion)	79.5 ± 16% SD	30.1 ± 9% SD	39.5 ± 10% SD
Saline Circulation	78.3 ± 15% SD	25.0 ± 14% SD	34.4 ± 12% SD
Ox—N Circulation	47.4* ± 17% SD	12.8* ± 2% SD	19.2* ± 10% SD

Table I - Percentages are expressed in terms of total tissue area lesions by hemmorhagic necrosis for grey, white or total cord area two hours after severe injury with the various treatments. (*Statistical Significance $P = < 0.01$. The saline values are not significant).

The data indicates a highly significant degree of protection against injury lesions afforded by the Ox-N circulation treatments. The actual lesions are halved by the treatment and this remarkable stabilizing effect upon the important white matter tracts would be anticipated to substantially improve the final functional result attending severe spinal cord injury.

Anterior Horn Cells

A technique of counting the anterior horn cells which contain visible acid phosphatase histomchemical reaction product has been developed in this laboratory. The procedure has been previously used to assess ischemic cellular effects in terms of cellular survival and/or lysis time.

From Table II it can be seen that untreated injury has a highly lethal effect upon anterior horn neurones. Within the two hour experimental time period, more than 97% of all cells at the injury center undergo cytoplasic lysis. Ox-N infusions stabilized the injured cells as 60% of all neurones were protected from lysis.

TABLE II

ANTERIOR HORN CELLS	
Control	34 ± 2 (SD)
Injury	2 ± 1.73*
Injury + Ox—N circulation	21 ± 5.12**

Table II - Number of anterior horn cells containing acid phosphatase reaction product within well defined cytoplasmic borders, (*statistical difference from control $P < 0.001$, **Difference from injury alone $P < 0.001$).

Spinal Cord Adenosine Triphosphate (ATP)

Biochemical ATP tissue determinations were undertaken to determine the metabolic oxidative state of injured spinal tissues. This metabolite was selected for study since it reflects the progress of normal oxidative metabolism. ATP levels fall very rapidly under sufficient hypoxic-ischemic conditions. Untreated injured cords have a 200% ATP decline in one minute. In the current experiments ATP levels would be expected to reflect (1) the cellular oxidative capability and (2) functional cellular viability. The latter aspect is especially important in terms of cellular integrity which was discussed in the preceeding section.

From Table III it can be seen that 2 hour injury causes a four and three fold drop in grey matter and

white matter ATP respectively. This information amply supports other observations about the degree of regional cord tissue ischemia after impaction. ATP was found in significantly higher concentration in the Ox-N experiments than noted after saline circulation alone. The high energy compound suffered only a 30% fall from normal in the oxygenated perfusion group which contrasts vividly with the 300–400% loss found with the saline treatments.

TABLE III

ATP LEVELS (μmol/gm) (2 hours post injury)			
	Injury & Saline	Injury & Ox—N	Control
Grey Matter	0.46	1.24*	1.88
White Matter	0.40	0.87*	1.23

Table III - ATP tissue levels in control, saline and Ox—N injured cords. The difference between saline and Ox—N is significant *($P = 0.05$). Although not shown in the Table, the Ox—N treatments also statistically increase ATP in spinal cord regions directly above ($P < 0.001$) the injury site.

Comparison of the above results to those later reported by R. E. Hanseabout, R. H. C. Van Der Jagt, S. S. Sohal, and J. R. Little, *Journal of Neurosurgery* 55, pp. 725–732 (1981) is of interest. Hanseabout et al report the use of a commercial oxygenated fluorocarbon artificial blood perfusate to treat experimental spinal cord injuries. Treated dogs are reported as showing improved motor function more rapidly and as having a better final hind limb functional result than did controls. To some extent, this non-prior art report confirms the spinal cord injury findings reported here.

EXAMPLE 3

Cerebrovascular Ischemia

Initial studies have been conducted to determine the efficiency of Ox-N emulsions in protecting the brain against profound ischemia. We employed the cat brain and utilized right hemispheric regional vascular interruption so that the left cerebral hemisphere might serve as an internal control. The middle cerebral artery of cat is accessible through the bony orbit. It lies immediately above the optic nerve after the canal has been opened and can be identified with certainty in that position. Preliminary experiments determined that an inconstant cerebral field was devascularized by occluding the middle cerebral artery. It became apparent that collateral blood flow via the anterior and posterior cerebral arteries supplied some retrograde filling into the experimental region. This phenomenon could be largely prevented by concommittantly reducing the mean systemic blood pressure to 70 mmHg by external bleeding. Hemorrhagic hypotension plus middle cerebral artery occulsion yielded a reasonably constant ischemic cerebral lesion from animal to animal.

In that model either saline or Ox-N were circulated from the right cerebral ventricle to the cisterna magna at a rate of 3 ml/min. Cerebral tissues were harvested one hour after vascular occlusion by immediate immersion in liquid Freon. The tissues were sectioned in the frozen state and reacted with luciferin upon photographic film. A combination of high energy cellular metabolites plus luciferin react to emit visible light, which is recorded upon the film. Tissues removed from saline treated ischemic cerebral regions were uniquely devoid of phospholuminescence, while the opposite hemisphere demonstrated this reaction to a degree similiar to that found in normal animals. Middle cerebral ischemic tissue samples from Ox-N treated animals contained sufficient high energy materials to demonstrate a positive histochemical high energy reaction one hour after vascular arrest.

EXAMPLE 4

Profound Spinal Cord Ischemia

The combined evidence from spinal cord injury and middle cerebral artery occlusion models demonstrate that the preferred oxygenated nutrient emulsion can be circulated to maintain cellular integrity and aerobic metabolism under the stress of profound regional ischemia. A third model was utilized to determine if vascular deprived neurones perfused via cerebrospinal fluid pathways with oxygenated-nutrient would continue to perform a physiologic function. A transthoracic aortic ligation just distal to the left subclavian effectively devascularizes the cervical, thoracic and lumbar cat spinal cord. In some examples the lower brain stem was also found ischemic by regional flow studies. The mid and lower thoracic cord are universally and profoundly blood deprived by this vascular interruption. Animals under light Ketamine anesthesia were treated by circulating from the lumbar subarachnoid space to the cisterna magna with either saline or Ox-N solutions. Respiratory movements were evaluated in these experiments. The lungs were ventilated by positive presence respiration, but the mechanical movements are easily distinguished from neuromuscular respiratory contractions. This is especially so since for the most part the respiration and neuromuscular drive occur at separate times and are largely asynchronous. Following the aorta ligation all physiologic neuromuscular respiratory movements progressively diminished to total cessation after 5–10 minutes in the saline treated cats. The arrest obtains for intercostal muscles as well as diaphragmatic contractions. The Ox-N treated animals, on the other hand, continue to respire in an essentially normal neuromuscular sequence. The respiration, under those conditions, were often of irregular rates, diminished in amplitude, and showed some individual magnitude variations. The singular difference between saline and Ox-N circulations is the universal persistence of respiration in the latter group. It is also true that Ox-N sustained sufficient chest bellow movements so that if the chest were closed the respirations were clinically adequate to support life.

EXAMPLE 5

Experiments have also been conducted to determine the efficacy of the herein disclosed methods on global cerebral ischemia induced in cats.

Although the Ox-N emulsions of the present invention are oxygenatable by bubbling gas through them, perfusate from stroke animals were initially found to have oxygen pressures (pO_2) below those known efficient oxygen exchange values (pO_2 less than 200) for the fluorocarbon component of the material. See Navari et al, supra. Accordingly, the pump oxygenation system described above in connection with FIG. 13 was developed to optimize fluorocarbon O_2 saturation. As mentioned above, this system comprises a heat exchange-oxygenator which was coupled to recirculating, warming and delivery pumps. This system rapidly oxygenates the emulsion (pO_2=645[mean] Torr) at 37° C. with oxygen gas delivered at 7 L/min.

Global cerebral ischemia experiments were conducted on cats after brevital induction and nitrous oxide oxygen (70–30%) anesthesia. A double lumen inflow

cannula of the type described above was sterotactically placed into a lateral cerebral ventricle while an exit cannula was inserted either into the cisterna magna or lumbar theca. When the conduits are properly installed, the CSF pathways have little resistance and a mean flow perfursion rate of 6.0 cc/min. can be achieved through the animals without intracranial pressure alterations. Entry and exit fluid were collected for metabolic studies. Both gases were normalized by respiratory adjustment. Further experimental manipulations awaited electroencephalograph (EEG) normalization. Cerebral ischemia was produced by the combined insult of hemorrhagic hypotension (mean arterial blood pressure lowered to 30±3 mm Hg) plus simultaneous carotid artery clamping. This method caused a bihemispheric isoelectric EEG within 5–8 minutes. After sustained and total cerebral electro silience for 15 minutes, the carotid arteries were unclamped and the withdrawn blood reinfused.

A well accepted measure of cerebral function, the EEG, was used to assess both the degree of insult and subsequent discovery. A computer based EEG method, compressed spectral analysis, was used to determine brain activity. A Nicolet Instrument Corporation "MED-80" computer utilizing frequency analysis package "Super C" was used with the following setup parameters:

2 channels, 1024 SEC. EPOCH, 1024/PTS.EPOCH
2 sweep average/printout.

The total output is expressed in (microvolts^2) assuming a constant source impedence of 1 ohm. The data presented here is the total cerebral power 0.3–25 Hz in picowatts. Recordings were made from skull electrodes at maximum sensitivity of 1 picowatt. Since a steady state prestroke EEG was obtained, each animal served as its own control.

Ten animals had cannulas placed and the stroke accomplished without perfusion. A second control group of ten animals were treated similarly, but were also perfused through the ventriculo spinal (lumbar) route with nutrient solution without fluorocarbon. There were no apparent differences found for post-stroke electroencephalographic activity in these groups. As a measure of stroke severity, 13 animals (of 20) had persisting electrocerebral silience. Of the remaining animals, 5 gained only 2% of their base line power while two had 10% power return within the 4 hour experimental period. FIG. 4 is a representative EEG power tracing from the left and right cerebral hemispheres of a cat perfused only with nutrient solution without fluorocarbon and which exhibited persisting electro-cerebral silience during the 4 hour experimental period. The tracings are read from bottom upwards. Normal activity is seen in the lowest tracing and is totally arrested by the ischemic insult half way through the first grouping. There is electro-cerebral silience thereafter througout the experimental period.

Thirteen cats underwent the same experimental procedure, but were perfused immediately after ischemia with bubble oxygenated nutrient solution (pO_2=400). For these cats, the flow rate was 4 ml/min with withdrawal from the umbar theca. Five exhibited continued electro-silience whereas 8 demonstrated EEG recovery from 5% (6 animals) up to 34% (2 animals). FIG. 5 is a representative EEG tracing of one of the eight animals demonstrating 5% recovery after perfusion with oxygenated nutrient emulsion (pO_2=400).

A fourth group of 7 cats was perfused with pump oxygenated nutrient solution (pO_2=645) at 6 ml/min. with withdrawal from the cisterna magna. All cats in this group regained some electrocerebral activity. The final total power which returned ranged from 5 to 88% of the prestroke base line (average 22%; $p<0.01$ compared to all non-oxygen groups). The electroencephalographic activity recovered generally throughout the 4 hour recovery period with the returning total cerebral power exhibiting a first order relationship as a function of time. At the observed recovery rate all animals should achieve completely normal EEG power spectra within 8 hours. An oxygen dependent EEG response is seen when non-oxygenated, bubble oxygenated (pO_2=400), and pump oxygenated (pO_2 =645) groups are compared as electrocerebral activity recovery greater than 5% was found in 10%, 62% and 100% respectively. FIG. 6 is an EEG tracing of the animal showing 88% return of electrocerebral activity within 4 hours after perfusion with oxygenated nutrient emulsion (pO_2=645). The asymmetry between hemispheres is an individual variation for this animal.

FIG. 7 is a portion of an EEG tracing showing the recorded effect on electro-cerbral activity of a temporary perfusion failure. This animal, which was perfused using the pump-oxygenated (pO_2=645) nutrient emulsion described above, experienced an interruption (pt. A) in perfusion for a time period of approximately 1 hour, whereupon perfusion was resumed (pt. B). As seen in this tracing a major deterioration of EEG activity occurred following cessation of perfusion, and resumed thereafter, confirming that the present method in fact sustains EEG activity.

In FIG. 8, the effect of a diminished perfusion flow rate of oxygenated nutrient emulsion is shown on the rate of glucose metabolism, and lactate and pyruvate concentration. In accordance with the above-described ventriculo-lumbar perfusion procedure using bubbled oxygenated (pO_2=400) nutrient emulsion, flow rate with nutrient emulsion without fluorocarbon was established at about 5.0 ml/min. A base line cerebral metabolic rate of glucose metabolism (CMRGl) was established prior to stroke, which was followed after 15 minutes with the perfusion of the oxygenated nutrient emulsion. CMRGl, which has recovered somewhat after 1 hour, is seen to decline rapidly as the flow rate of perfusate declines. Similarly, lactate levels rise precipitiously with flow rate decay. These results once again confirm that the flow of oxygenated nutrient emulsion through the cerebral spinal pathway should be maintained at acceptable rates in order to sustain neurologic tissue.

In FIG. 9, the mean recovery percent for the four groups of animals discussed above is presented in the form of a bar graph. It is presently preferred to insure that the pO_2 value of oxygenated nutrient emulsion upon input is great enough to insure that efficient oxygen transfer capabilities are maintained at the selected flow rate. For the FC lumbar group, exposure of oxygenated nutrient solution to certain tissue regions when its oxygen exchange value was below the known efficient oxygen exchange value (pO_2 less than 200) for the fluorocarbon component of this material may have occurred. This may be true even though the mean oxygen exchange value of the withdrawn emulsion is above 200. Accordingly, it is presently preferred to maintain the pO_2 value of withdrawn oxygenated nutrient emulsion at twice this minimum, or at above 400, either by

raising the input pO_2 value to much higher levels, as with the ventriculo-cisternal animals described above, or by increasing the flow rate of oxygenated nutrient emulsion through the animal to maintain those values. In smaller animals, such as cats, the size of the cerebro spinal pathways creates hydraulic resistance which limits the flow rates which may be achieved at atmospheric pressures using certain pathways. In such animals, higher oxygen exchange values and shorter perfusion routes, such as the ventriculo-cisternal perfusion route, are preferred. In larger animals, such as humans, it is not anticipated that flow rates will be so limited. Nonetheless, high pO_2 values (at least 50% preferably 80+% of the maximum obtainable pO_2) are preferred to minimize the volume of perfusate necessary to perform a given treatment and to provide an additional margin of safety at the selected flow rate.

Samples of the perfusing fluids for the animals of this example were removed at predetermined times from entry and exit perfusion ports for analysis of lactate and pyruvate under a single blind condition. The results are summarzied in Table IV:

TABLE IV

Levels of lactate and pyruvate in cerebral spinal fluid perfusate before (baseline), during (isoelectric) and following (reflow) global ischemia in cats. Data are expressed in mg per 100 ml of perfusate and the values are means ± standard error. Six animals were perfused with NS[1] and 7 with OFNS[2] solution. After collecting the perfusate in tubes a 4#C, the samples were stored at −80° C. for analysis. Lactate and Pyruvate were assayed by a Sigma Method (Sigma Technical Bulletin #726, Oct. 1968 and #862, Oct. 1969) and conducted by Jefferson University Clinical Laboratories.

Experimental Period	Lactate		Pyruvate		Lactate/ Pyruvate Ratio	
Baseline+	3.6 ± 1.1*		0.5 ± 0.1		7.2	
Isoelectric+	8.1 ± 1.9*		0.5 ± 0.1		16.2	
	NS	OFNS	NS	OFNS	NS	OFNS
Reflow (5 min)	21.9 ± 11	10.0 ± 1.0	0.5 ± 0.1	1.2 ± 0.6	43.8	8.3+
Reflow (4 hr)	8.9 ± 3.3	10.4 ± 3.8	0.5 ± 0.1	1.7 ± 0.7	17.8	6.1

*During baseline and isoelectric time periods all cats were perfused with NS.
+$p < 0.01$ when compared to baseline lactate. $p < 0.025$ when compared to the ratio of reflow (5 min) perfused with NS.
[1]As used herein, NS refers to the nutrient solution of Example 1 without fluorocarbon component.
[2]As used herein, OFNS refers to the preferred oxygenated, fluorocarbon nutrient emulsion of Example 1.

In animals perfused with nutrient solution without fluorocarbon the concentration of lactate during the actual stroke (isoelectro) was of the normal CSF value. The lactate level rose percipitiously, an additional 440%, within 5 minutes of restoring the blood pressure and blood flow through the carotid arteries. Thereafter the level declined during the 4 hour period to 147% of base line. In contrast to the lactate data, the pyruvate concentration remained constant through the perfusion period.

When animals were perfused with oxygenated nutrient emulsion, on the other hand, the percipitious increase in lactate did not occur; instead there was a modest 52% rise during the initial 5 minute period, and the level thereafter remained stable. Significantly, in the oxygenated series the concentration of pyruvate more than doubled during the initial 5 minutes and continued to increase gradually during the remainder of the 4 hour period. The net production of lactate and pyruvate are often used as indictators of anarobic and aerobic glycolysis, respectively. Since these compounds change under different circumstances the expression of lactate/pyruvate (L/P) ratio best illustrates the net metabolic effects. A high L/P ratio indicates that anarobic glycolysis predominates. It is common practice, therefore, to use the L/P ratio as a sensitive indicator of the redox state of cells. Perfusion oxygenation in accordance with the present inventions significantly ($p \leqq 0.01$) lowered the L/P ratio when compared to non-oxygenation (8.3 vs. 43.8). It is further evident that the oxygenated 4 hour L/P ratio is additionally lowered, whereas the non-oxygenated values are still 5 times greater than the control.

Although the oxygenated nutrient perfusate transit time through the brain is only a few seconds, significant oxygen extraction does occur. It was determined by the pO_2 difference between inflow and outflow fluids that oxygenated nutrient emulsion lost pO_2=210 (mean) during its intracerebral passage. Also unique to the oxygenated nutrient emulsion studies was a rising carbon dioxide presence in the exit fluid which did not occur in non-oxygenated experiments. The pCO_2 rose 5 fold in these fluids over the four hour period (pCO_2=6.0 vs. 3.0). It is considered that the appearance of carbon dioxide is important since it is a normal product of aerobic metabolism.

In FIGS. **10** and **11** levels of potassium in perfusate before (base line), during (isoelectric) and following (reflow) global cerebral ischemia in cats are represented. Data are expressed in micro equivalents per minute, and the values are means ± standard error. Five animals were perfused with nutrient emulsion without fluorocarbon, and six with oxygenated fluorocarbon emulsion. After collecting the perfusate in tubes at 4° C., the samples were stored at −80° C. for analysis. Potassiums were assayed by atomic absorption spectrophotometry. During the base line and isoelectric time periods, all 11 cats were perfused with nutrient emulsion without fluorocarbon. There were no significant differences between isoelectric and base line levels of potassium in the perfusate. As seen from FIGS. **10** and **11**, significant differences in the values of potassium were observed beginning almost immediately with perfusion (at time 0) and extending throughout the 4 hour experimental period.

FIG. **12** discloses the effects on glucose metabolism for ventriculo-cisterna perfused animals subjected to the stroke and reperfusion procedure of this example. In accordance with the invention of Dr. John Lewis Alderman, one of these animals was perfused with twice

the glucose concentration (372 mg %) of that used for the remaining animals described herein. As seen from FIG. 12, the glucose metabolism of animals provided with oxygenated nutrient emulsion (glucose =186 mg %) is generally superior following reperfusion to the metabolism rate of the control receiving that solution without fluorocarbon. In view of the substantial increase in glucose metabolism exhibited by the animal having a "double glucose" solution (372 mg %), it is presently preferred to include at least such elevated glucose concentrations in perfusions performed in accordance with the method of the present invention.

These experimental results demonstrate that extravascular perfusion of oxygenated nutrient emulsion affects a significant reversal of the adverse cerebral metabolic effects induced by the experimental stroke condition. Coincident with the improve metabolic state electrocerebral activity returned. These findings indicate that extravascularly supplied oxygen, glucose and other nutrients were taken up and metabolized in amounts sufficient to restore high energy compounds and thereby reactivate membrane ionic pumps and reinstitute electrocerebral activity.

Oxygenated-fluorocarbon-nutrient-emulsion caused no detrimental effects on vital physiologic functions such as heart rate, blood pressure or electrocerebral (EEG) activity when perfused through the ventricular system for four hours of cats not subjected to the stroke paradigm. These animals exhibited no ill effects after 5–8 months, and were killed for a double blind neuropathologic examination of the brain, spinal cord and subarachnoid spaces. No gross or microscopic changes were observed and the specimens were indistinguishable from non-perfused animals.

In view of the above, those of ordinary skill in the art will recognize that various modifications can be made to the methods and apparatus described above without departing from the scope of the present invention. For example, it should be understood that, the injection and withdrawal catheters used to perform the herein described method should be sealed with respect to the skull so that a water and bacteria tight seal is created between these catheter and skull. Although conventional bone wax has been used for creating this seal in the feline experiments described above, fitting 22(*a*) preferably comprises a double threaded sleeve which is threaded into a bone aperture, and in turn receives complimental threads formed on injection catheter 20*a*. Such attachment means, particularly when used with a ventricular injection catheter, should eliminate any need for total head immobilization during human treatment.

It should also be understood that the oxygenated nutrient emulsions of the present invention may contain various therapeutic agents including free fatty acids, prostaglandins, prostacyclins, cyclic nucleotides and hormones.

As seen from the above, it is desired to maintain the the pO_2 level in the withdrawn fluid at levels which are substantially above the minimum level of efficient oxygen exchange of the subject fluorocarbon. For the fluorocarbon nutrient emulsion described above, that minimum (unsaturated condition) occurs at a pO_2 equal to about 190, which is about 30% of the readily achieved maximum pO_2 level. (pO_2=645) As described above, it is preferred to perform the treatment method of this invention so as to maintain the pO_2 of the withdrawn oxygenated nutrient emulsion at a pO_2 above 400, that is, at a pO_2 level which is about twice the minimum level of efficient oxygen exchange for the subject fluorocarbon. It is presently anticipated that a similar differential should be maintained in practicing the present invention utilizing oxygenated nutrient emulsions having other oxygenatable components exhibiting different ranges of efficient oxygen exchange.

The methodology described requires the formulation of a physiochemical fluid which must be adequately oxygenated, temperature controlled and delivered under well controlled conditions. The perfusion system of the present invention may be routinely placed by trained animal surgeons. Neurosurgeons commonly possess skills necessary to implant treatment ports in accordance with the present invention in humans. The procedure is relatively simple and can be quickly accomplished with available instruments. The oxygenated nutrient emulsion treatment delivery system of the present invention has certain similarities to the arterial heart-lung machine. Major differences, however, include the use of a complex synthetic fluid for cerebral spinal perfusion, the route performed by cerebral spinal perfusion is an extravascular one, and there is no known limitation on perfusion time in accordance with the herein disclosed method. Oxygenated fluorocarbon nutrient emulsion tolerates pumping mechanics well and the exit fluid can either be discarded or recirculated. Formed blood elements, on the other hand, are fragile and lyse under prolonged recirculation conditions. It is presently contemplated that cerebral-spinal fluid perfusion support will need to be carried out until the vascular system can once again take over. Surgical revascularization or bypass procedures will in some cases be necessary to accomplish this end. The return of cerebral vascular compentency can be assessed by measurements of regional blood flow, electro cerebral activity, and the metabolic configuration of the exit perfusion fluid. One foreseeable complication of this technique is bacterial infection, and rigorous attention to ambient sterility, millipore filtering, and antibiotics should reduce this hazard to acceptable levels. Safeguards have been built into the pumping system to immediately stop delivery if either the inlet or outlet become obstructed.

Conclusion

As seen from the above examples, and the foregoing description, circulation of the preferred embodiment nutrient liquid is capable of sustaining cellular integrity, aerobic metabolism and ongoing neuronal function. Even for neurons deep within the spinal cord (grey matter) the process has been successful in nurturing the ischemic neurons. The ability to sustain the central nervous system in a lethally ischemic field which persists for longer than a few minutes has never been accomplished before. The extravascular pathway has not been employed as a global nutrient route prior to the present invention, nor has the combined use of oxygen rich emulsion which also contains the other disclosed novel components been know to the art.

As seen from the above experiments, the methods, compositions and system of the present invention are capable of providing substantial amounts of oxygen to neurologic tissues to be treated, while at the same time, removing the by-products of aerobic metabolism, including carbon dioxide, which have been found to exist in substantially higher concentrations in the exit, diagnostic fluid. Similarly, as discussed above, rapid, nor-

mally lethal, lyses of anterior horn cells is readily preventable through the treatment of the present invention, protecting at least 60% of the cells through this modality. Similarly, high energy phosphate metabolism utilizing both oxygen and glucose is maintained at substantial levels. Accordingly, the methodology of the present invention represents a substantial advance in the treatment of central nervous system tissue. Prior to this invention there was not a method available to sustain central nervous tissues after a few minutes of profound ischemic insult. This invention should revolutionize the therapeutic capabilities by providing therapeutic approaches for stroke, aneurysm, brain injury, vasospasm, senility, tumors, coma, spinal cord injury, ischemia, post shock, post cardiac arrest and central nervous system poisoning.

It is further anticipated that the treatment method of the present invention should make it possible to interrupt the cerebral blood supply with some impunity for surgical maneuvers not heretofore possible without great attendant risk of producing cerebral infarction. Those of ordinary skill in the art will recognize that future development may result in perfection of the oxygenated nutrient emulsion composition, delivery rates, treatment times, the width of the therapeutic window in which treatment may be instituted and the correlation of behavioral functions in surviving animals with normalization of cerebral chemistry and electrographic activity. Nonetheless, by any standard, the present invention provides a dramatic, yet clinically acceptable, therapeutic method for treating ischemic neurologic tissue.

What is claimed is:

1. A method of diagnosing the condition of suspected hypoxic-ischemic central nervous system tissue of a mammal, comprising:

(a) providing a synthetic spinal fluid comprising at least one oxygenated oxygen-carrying component and essential electrolytes to compatibilize the oxygen-carrying component for use with central nervous system tissue;

(b) injecting said synthetic spinal fluid into at least a first portion of the cerebrospinal pathway of said mammal to contact said tissue to become a diagnostic fluid;

(c) withdrawing said diagnostic fluid from a second portion of said pathway to create a circulation of said fluid through at least a portion of said pathway;

(d) monitoring the composition of said diagnostic fluid; and

(e) comparing constituents of said fluid for at least a selected difference in the compositions of said synthetic spinal and diagnostic fluids;

whereby said selected differences in said compositions are at least diagnostic of the condition of said suspected hypoxic-ischemic tissue disposed along said portion of said cerebrospinal pathway.

2. The invention of claim 1 wherein said selected difference is a difference in oxygen content.

3. The invention of claim 1 wherein said selected difference is a difference in lactic acid concentration.

4. The invention of claim 1 wherein said selected difference is a difference in carbon dioxide concentration.

5. The invention of claim 1 wherein said selected difference is a difference in ammonia concentration.

6. The invention of claim 1 wherein said selected difference is a difference in enzyme content.

7. The invention of claim 1 wherein said difference is a difference in pH.

8. The invention of claim 1 wherein said difference is a difference in GABA.

9. The invention of claim 1 wherein said difference is a difference in microorganism content.

10. The invention of claim 9 wherein said microorganism content is a bacterial content.

11. The invention of claim 1 wherein said difference is a difference in ion concentration.

12. The invention of claim 11 wherein said ion concentration difference is a sodium ion concentration difference.

13. The invention of claim 11 wherein said difference is the difference in the concentration of potassium ions.

14. The invention of claim 1 wherein said difference is a difference in amino acid concentration.

15. The invention of claim 1 wherein said difference is a difference in concentration of malignant cells.

16. The invention of claim 1 wherein said difference is a difference in concentration of myelin fragments.

17. The invention of claim 1 wherein said difference is a difference in identifiable cellular materials.

18. The invention of claim 1 wherein said difference is a difference in concentration of identifiable cellular organelles.

19. The invention of claim 1 wherein said difference is a difference in protein.

20. The invention of claim 1 wherein said difference is a difference in fats.

21. The invention of claim 1 wherein said difference is a difference in fat content.

22. The invention of claim 1 wherein said difference is a difference in RNA content.

23. The invention of claim 1 wherein said difference is a difference in DNA content.

24. The invention of claim 1 wherein said difference is a difference in cellular metabolic products.

25. The invention of claim 1 wherein said difference is a difference in metabolite content.

26. The invention of claim 1 wherein said difference is a difference in neurotransmitter content.

* * * * *

United States Patent [19]

Leonard

[11] **3,927,980**

[45] **Dec. 23, 1975**

[54] **OXYGEN OVERPRESSURE PROTECTION SYSTEM FOR MEMBRANE-TYPE BLOOD OXYGENATORS**

[75] Inventor: **Ronald James Leonard**, Elk Grove Village, Ill.

[73] Assignee: **Baxter Laboratories, Inc.**, Deerfield, Ill.

[22] Filed: **Aug. 22, 1973**

[21] Appl. No.: **390,567**

[52] **U.S. Cl.** **23/258.5**; 55/158; 128/DIG. 3; 195/1.8

[51] **Int. Cl.²** **A61M 1/03**

[58] **Field of Search** 23/258.5; 128/DIG. 3; 55/158; 195/1.8

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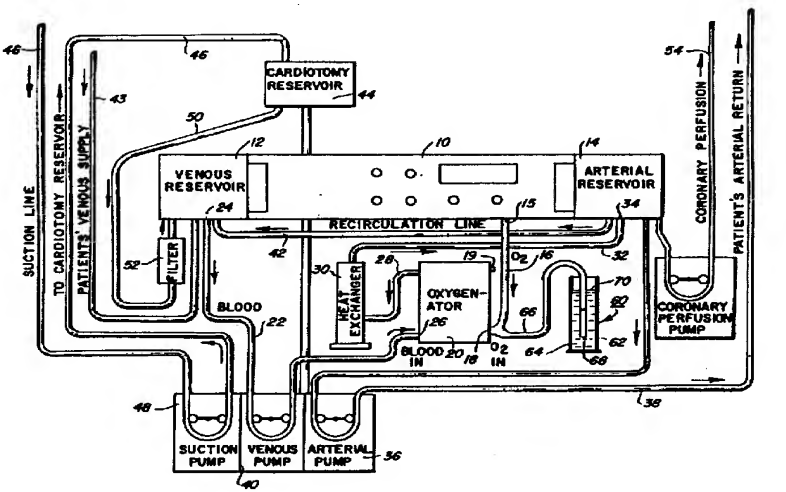
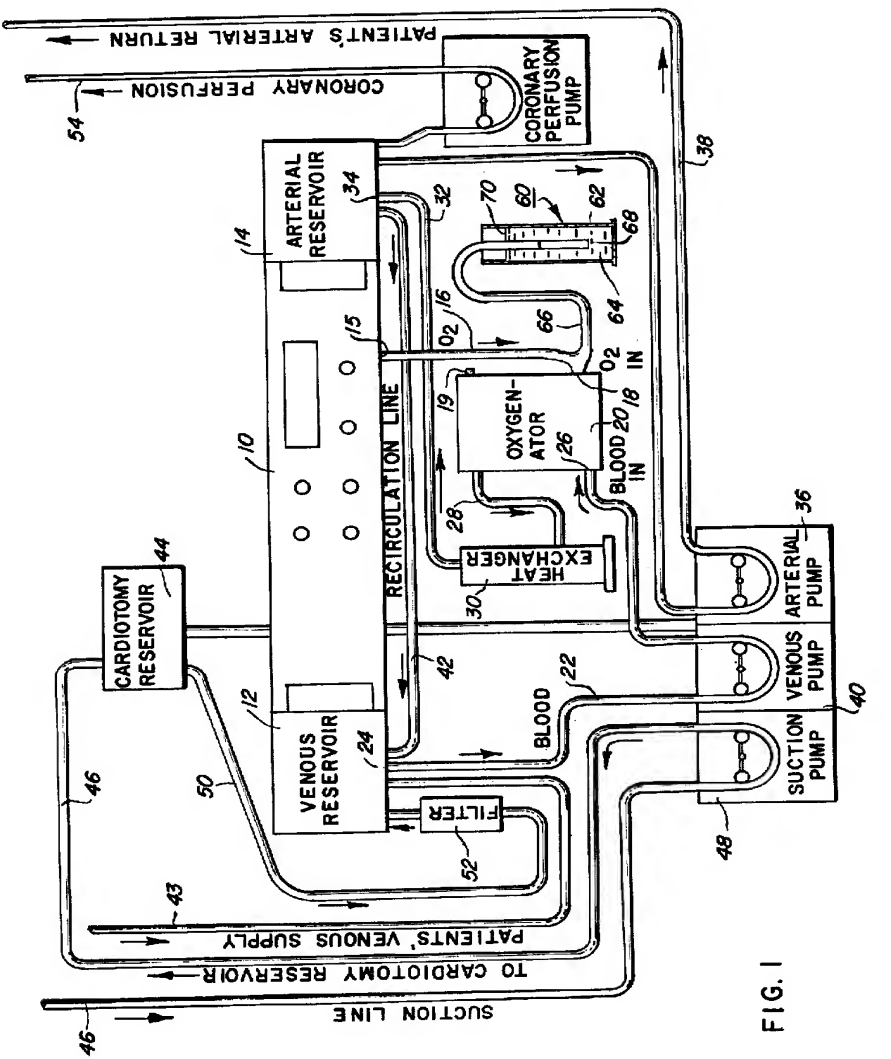
Primary Examiner—Barry S. Richman
Attorney, Agent, or Firm—Louis Altman

[57] **ABSTRACT**

A safety system is provided for a membrane-type blood oxygenator to prevent the possibility of gas embolism through the membranous barrier which separates the blood and the oxygen. The safety system includes a blood reservoir positioned at a higher horizontal level than the blood inlet of the oxygenator, so that a gravity head is maintained. In addition, a manometer is provided which has a fluid level to permit venting of the oxygen if the oxygen pressure exceeds a predetermined gas pressure, which gas pressure is lower than the minimum pressure of the blood in the oxygenator.

6 Claims, 2 Drawing Figures




PATIENT'S ARTERIAL RETURN
CORONARY PERFUSION
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CORONARY PERFUSION PUMP
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ARTERIAL RESERVOIR
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O_2 IN
19
OXYGEN-ATOR
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RECIRCULATION LINE
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HEAT EXCHANGER
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ARTERIAL PUMP
CARDIOTOMY RESERVOIR
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PATIENTS' VENOUS SUPPLY
TO CARDIOTOMY RESERVOIR
SUCTION LINE
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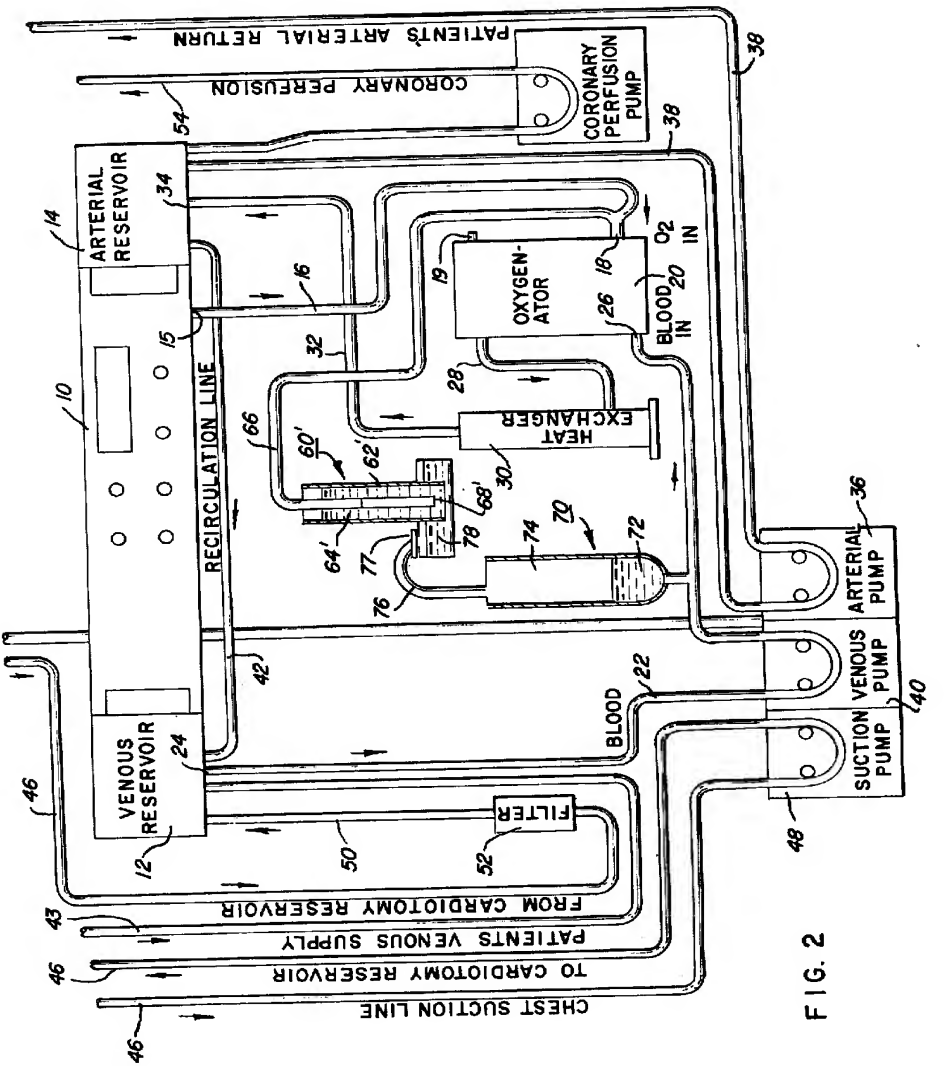
FIG. 1


PATIENTS ARTERIAL RETURN
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PATIENTS VENOUS SUPPLY
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FIG. 2

OXYGEN OVERPRESSURE PROTECTION SYSTEM FOR MEMBRANE-TYPE BLOOD OXYGENATORS

BACKGROUND OF THE INVENTION

This invention relates to a safety device for a mass transfer system, and more particularly, to a system for preventing an excessive amount of gas from transferring to a liquid on the opposite side of a membranous barrier.

The system of the present invention is particularly useful as a gas embolism protection system for extracorporeal oxygenators of blood in which both oxygen and carbon dioxide are transferred across a membranous barrier separating the blood and the oxygen. An exemplary oxygenator with which the present invention can be effectively utilized is disclosed in the United States patent application in the name of Ronald J. Leonard, Ser. No. 170,163, filed Aug. 9, 1971 and now U.S. Pat. No. 3,757,9.. It is to be understood, however, that the present invention may be utilized with many different types of mass transfer devices, particularly those using a porous hydrophobic membranous barrier separating a liquid and a gas.

The advent of controlled pore size, nonwetting, microporous membranes has made the construction of high transfer rate membrane oxygenators possible. The membranes have open pores which permit relatively rapid transfer of oxygen, yet the nonwetting properties prevent blood loss from the system. During operation of the oxygenator, it is important that the blood pressures exceed the oxygen pressures, because accidental reversal of oxygen and blood pressures might result in large amounts of oxygen rapidly entering the blood spaces of the oxygenator. In high flow rate oxygenators, the rapid oxygen accumulation would overwhelm any reservoir or bubble trap and allow gas to enter the patient. The sizes of reservoirs or bubble traps are limited as a result of the need to limit priming volume.

Extracorporeal oxygenators generally require a relatively high gas volumetric flow rate, and it is important for the gas spaces to be compact, with good mixing, in order to ensure effective gas transfer through the microporous membrane. Since this results in some gas pressure drop in the oxygenator, gas working pressures are generally greater than atmospheric. It can be seen that if the blood pressure were reduced to zero, the gas pressure would be greater than the blood pressure. Such a reversal of gas and blood pressures could easily occur at idle condition when there is no blood flow in the oxygenator.

It is extremely difficult, if not impossible, for an operator to maintain the variable pressures in an oxygenator in the proper direction. It is thus an object of the present invention to provide an automatic system of pressure control for a mass transfer system such as an oxygenator.

It is a further object of the present invention to provide a system for preventing accidental reversal of gas and liquid pressures in a mass transfer system without utilizing devices which have moving parts, springs, small orifices, or diaphragms which can become disabled or plugged up, thereby causing system failure.

Other objects and advantages of the present invention will become apparent as the description proceeds.

BRIEF DESCRIPTION OF THE INVENTION

In accordance with the present invention, a safety system is provided for a mass transfer system of the type wherein a membranous barrier separates a liquid and a gas, and including a liquid inlet, a liquid outlet, and a gas inlet and outlet. The improvement comprises means for maintaining at all times a liquid pressure which is higher than the gas pressure. A gas pressure sensing device is coupled to the gas inlet with the gas pressure sensing device comprising means for venting the gas, to prevent the pressure of the gas from exceeding the pressure of the liquid.

In the illustrative embodiments of the invention, the liquid pressure maintaining means comprises a liquid reservoir positioned at a higher horizontal level than the liquid inlet, whereby gravity liquid pressure is maintained. A first pump is located downstream of the reservoir for drawing liquid therefrom, with the reservoir being collapsible to prevent a negative pressure on the mass transfer device if the pumping action is excessive.

In the illustrative embodiments of the invention, the gas pressure sensing device comprises a manometer having a fluid level that prevents gas from venting unless the gas pressure exceeds a predetermined maximum gas pressure. The fluid level of the manometer is such that it permits gas to vent if the gas pressure exceeds the maximum gas pressure, with the maximum gas pressure being a pressure that is lower than the minimum pressure of the liquid in the oxygenator.

In one embodiment of the invention, another manometer is provided, and is operable in response to a pressure of the liquid for variably adjusting the first-mentioned manometer.

A more detailed explanation of the invention is provided in the following description and claims, and is illustrated in the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic flow diagram of a safety fluid flow system for mass transfer devices in accordance with the principles of the present invention.

FIG. 2 is a schematic flow diagram of a modified safety fluid flow system for mass transfer devices according to a second embodiment of the present invention.

DETAILED DESCRIPTION OF THE ILLUSTRATIVE EMBODIMENTS

Referring to FIG. 1, a mass transfer system is shown therein in the form of an extracorporeal oxygenator system, including a main console **10** to which a venous reservoir **12** and an arterial reservoir **14** are attached. Console **10** has an oxygen outlet **15** to which a conduit **16** is connected to feed a regulated flow of oxygen to the inlet **18** of an oxygenator **20**. After passing through oxygenator **20**, the spent gas exits via outlet **19**. Main console **10** contains a gas flow rotometer, an oxygenator shim pressure control, a temperature readout meter, and the necessary selector buttons and switches, all as is well-known in the art. Console **10** is located to be within the operator's easy reach, but out of the way of possible fluid contamination.

Oxygenator **20** is a typical oxygenator wherein oxygen and carbon dioxide are transferred in opposite directions across a membranous barrier separating the blood and the oxygen. Such oxygenators are disclosed in the United States patent application in the name of

Ronald J. Leonard, Ser. No. 170,163, filed Aug. 3, 1971.

It is to be understood that the system of the present invention is particularly suitable for use with any oxygenator using a microporous hydrophobic membrane. A typical suitable membrane material is polytetrafluoroethylene sheeting having a pore size of less than 0.5 micron and being about 0.005 inch thick. Another exemplary membrane is formed of polypropylene sheeting approximately 0.001 inch thick and having a pore size of about 0.1 micron. The membranes can be laminated to screening for strengthening support.

A blood conduit **22** is connected from an outlet **24** of venous reservoir **12** to blood inlet **26** of oxygenator **20**. The blood and oxygen flow through oxygenator **20** on opposite sides of the membrane contained therewithin and the blood exits via conduit **28** to a heat exchanger **30**, which regulates the blood temperature. A typical heat exchanger which could be utilized with the system of the present invention is disclosed in Leonard et al. U.S. Pat. No. 3,640,340, issued Feb. 8, 1972. The blood is then returned via conduit **32** to an inlet **34** of arterial reservoir **14**.

An arterial pump **36** is utilized to pump oxygenated blood from arterial reservoir **14** via conduit **38** for flow to the patient's artery. A venous pump **40** is utilized to pump the blood from venous reservoir **12** to blood inlet **26**. Line **43** provides blood from the patient's venous supply to venous reservoir **12**. The two pumps (venous pump **40** and arterial pump **36**) aid to protect the oxygenator and heat exchanger from overpressurization. Venous pump **40** draws blood from venous reservoir **12** and propels it through oxygenator **20** and heat exchanger **30**, and into arterial reservoir **14**. Arterial pump **36** draws blood from arterial reservoir **14** and propels it back to an artery of the perfused subject.

Since the exact matching of the pumping rate of the two pumps is difficult, if not impossible, the venous pump **40** is set to run at a slightly greater speed than the arterial pump **14**. A recirculation line **42** between the arterial reservoir **14** and venous reservoir **12** allows the extra flow generated by venous pump **40** to return to the venous reservoir. This assures that the arterial reservoir **14** has blood in it at all times while protecting the oxygenator **20** from over-pressure due to blood accumulation.

Venous reservoir **12** and arterial reservoir **14** are preferably formed of a medical grade polyvinylchloride plastic, or silicone rubber, and are collapsible. Thus in the event the output of either venous pump **40** or arterial pump **36** exceeds the input into a reservoir, the respective reservoir collapses to restrict outflow, thereby preventing a reduced pressure from forming upstream of the reservoir. This is particularly important with respect to arterial reservoir **14** because it is necessary to maintain a minimum blood pressure on the oxygenator so long as there is blood in the system by maintaining a blood pressure head in conduits **22**, **32**, and **28**.

It is important that reservoir **14**, and preferably also reservoir **12**, is supported so that its lower edges are above the upper port of the oxygenator generally by at least about 3 inches. In this manner, a gravity-induced liquid pressure head is always exerted on the oxygenator by the blood in the reservoir. The gravity head of the blood is arranged as described below to be always greater than the gas pressure in the oxygenator, to guard against the possibility of gas bubbles passing through the microporous membrane.

A safe, positive, direct method of pressure control is provided by coupling to oxygen inlet **18** a gas pressure sensing means **60**. Gas pressure sensing means **60** comprises a manometer including an open container **62** having liquid **64**, such as water, filled to a predetermined level. A venting conduit **66** is coupled from oxygen inlet **18**, to the inside of container **62**, passing downwardly through the top of container **62**, to form the manometer construction. Fluid **64** is filled to that level which requires enough back pressure in venting conduit **66** to thereby prevent the gas from venting unless the gas pressure exceeds the predetermined maximum gas pressure, and to permit the gas to vent if the gas pressure exceeds such maximum gas pressure. The maximum gas pressure is selected to be a pressure that is lower than a pressure of the blood in the oxygenator created by the pressure head in line **34**, that is, lower than the pressure of the blood in the oxygenator at the vertically highest point of the blood flow path therein. Thus, the vertical distance between outlet **34** of reservoir **14** and oxygen inlet **18** of oxygenator **20** must be greater than the vertical distance between lower end **68** of conduit **66** and surface **70** of fluid **64**. In that manner, the gas pressure must always be lower than the blood head, which typically is about 18–19 inches minimum at inlet **26**. Thus gas cannot bubble through the membrane to enter the blood spaces. Typically, a 14 inch pressure head of water exists in manometer **60** when the gas pressure is sufficient to cause flow through line **66**. When gas is not flowing, the pressure head is slightly less, since then water resides within line **66**, lowering the liquid level in container **62**.

The system is fail-safe because if the fluid **64** were to evaporate, the gas would be vented at a lower pressure than before evaporation. Thus, evaporation of fluid **64** only permits the gas to vent at a lower pressure, and the oxygenator remains safe from the possibility of a gas embolism passing through the membrane.

A line **43** connected to the patient's venous blood supply feeds blood to venous reservoir **12**.

The system also may include a cardiotomy reservoir **44**, such as is shown in U.S. Pat. No. 3,507,395, the inlet of which is coupled to the incision site of the patient via suction line **46**. Blood spilled in the incision site of the patient is sucked by means of a suction pump **48** to which line **46** is connected. Conduit **50** couples the outlet of cardiotomy reservoir **44** to venous reservoir **12** through an optional auxiliary filter **52** which filters out any remaining clots and other gross particles in the blood, and then passes the blood to the venous reservoir. The cardiotomy reservoir is usually also located above the venous and arterial reservoirs to assist in providing a gravity head of blood.

Where coronary perfusion or other localized perfusion of an organ is desired, a perfusion conduit **54** is coupled to an outlet of arterial reservoir **14**, and the fluid is pumped through line **54** by means of a perfusion pump **56**.

A modified gas pressure sensing means is illustrated in FIG. **2**. As the remainder of the system may be identical to the FIG. **1** system, like reference numerals have been used for like structure. The gas pressure sensing means **60'** of FIG. **2** comprises a manometer formed by container **62'** and having an open top and bottom. Container **62'** contains fluid, such as water **64'**, and has oxygen line **66** inserted therein in a manner similar to

the previous embodiment. The manometer formed by container 62', fluid 64', and line 66 operates similarly to gas sensing means 60 of the FIG. 1 embodiment. However, the gas sensing means 60' of the FIG. 2 embodiment permits the maximum gas pressure to be raised if the blood pressure is raised, due to a change in blood flow rate or the like. However, it is still mandatory that the gas pressure be limited and remain less than the blood pressure. To this end, a closed blood manometer 70 is provided. Manometer 70 contains an amount of blood 72, which is dependent on the pressure in line 22, to which it is connected. This provides a variable gas pressure in the space 74 above blood 72 which also depends on the pressure in line 22. Hence, the height of fluid 64' is thereby dependent upon the pressure in space 74, tube 76, and line 22. The outlet of tube 76 communicates with sealed container 78, into which container 62' is positioned. A microporous plug 77 prevents blood from entering the control manometer 60' and provides a sterile barrier through which only the gas in space 74 and container 78 can pass. Plug 77 can be made of the same porous, hydrophobic membrane material as can be used in oxygenator 20.

It can be seen that a shift in the level of blood 72 will cause a pressure shift in space 74 and tube 76, thereby creating a fluid shift with respect to fluid 64'. Assuming that the blood pressure in line 22 is increased by an increased flow rate of other reason, the level of blood 72 will rise, thereby increasing the pressure in closed container 78. This will cause fluid 64 to rise in container 62', thereby permitting a higher oxygen pressure before venting from line 66 will occur. On the other hand, if the blood pressure in line 22 is decreased, the level of blood 72 in manometer 70 will be lowered, thereby decreasing the pressure upon fluid 64 and causing a drop in the height of fluid 64' within container 62'. Thus the gas will vent at a lower pressure as is required.

The above system provides additional efficiency coupled with safety, in that higher gas pressures may be used when higher blood pressures exist, but upon a sudden drop in blood pressure, the limiting maximum gas pressure will also drop to safe levels.

It is seen that an automatic system of pressure control has been provided for a mass transfer system, such as an oxygenator. The system is operative to prevent accidental reversal of gas and liquid pressures in a mass transfer system, without utilizing devices having moving parts, springs, small orifices, or diaphragms. The invention not only provides a safety system, but also permits effective operation of an oxygenation system at high altitudes, since manometers 60, 60' permit the safe use of gas pressures in an oxygenator which may exceed the ambient atmospheric pressure.

Furthermore, the use of manometers 60, 60' permit the continued lifesaving oxygenation of a patient even in the event of a gas delivery pressure valve failure or the like causing excess pressure, since the excess gas pressure is simply bled off by manometers 60, 60', while the oxygenator remains exposed to whatever predetermined maximum gas pressure has been selected.

Although two illustrative embodiments of the invention have been illustrated and described, it is to be understood that various modifications and substitutions may be made by those skilled in the art without departing from the novel spirit and scope of the present invention.

That which is claimed is:

1. In an extracorporeal oxygenator system wherein oxygen and carbon dioxide are transferred across a porous, hydrophobic membranous barrier separating the blood and the oxygen, said oxygenator having a blood inlet, a blood outlet, and an oxygen inlet and outlet; the improvement comprising, in combination: a blood reservoir coupled to said blood outlet downstream therefrom, said blood reservoir being positioned at a higher level than said blood outlet to provide to blood adjacent the membranous barrier a pre-determined minimum pressure; and manometer means which comprises an open liquid container being at least partially filled with a liquid; an oxygen supply line coupled to said oxygen inlet, venting conduit means coupled with said oxygen line and communicating with said liquid within said container and having an outlet therein, said liquid having a level that is selected to provide a pressure at said venting conduit means outlet but to permit venting of the oxygen in order to prevent the pressure of the oxygen from exceeding said minimum pressure of said blood.

2. An extracorporeal oxygenator system as described in claim 1, wherein the further improvement comprises said blood reservoir having an inlet and outlet for blood, and further including a first pump located downstream of and operatively connected to said outlet of said blood reservoir for drawing blood from said reservoir, said blood reservoir being collapsible to prevent a negative pressure upon the blood side of the oxygenator membranous barrier if the pumping action is excessive; and a second pump located upstream of and operatively connected to said blood inlet of said oxygenator for propelling blood to said blood inlet of said oxygenator said second pump being operated to pump at a greater flow rate than said first pump, and means for recirculating the extra flow of blood from upstream of said first pump to upstream of said second pump.

3. In an oxygen and blood delivery system for use in conjunction with a membrane-type blood oxygenator having a blood inlet and outlet and an oxygen inlet and outlet for diffusion therebetween across a porous, hydrophobic membrane, the improvement comprising:

blood and oxygen conduit means for operatively communicating with said respective blood and oxygen inlets and outlets of said oxygenator, and for conveying such materials to and from said oxygenator;

means for carrying a flexible blood reservoir in a position elevated above the position of said oxygenator,

receptacle means, open to the atmosphere, for containing a liquid;

an oxygen line having one end thereof disposed within said receptacle means, for immersion in liquid disposed in said receptacle means to create a predetermined pressure head at said one end, said oxygen line communicating with said oxygen conduit means, whereby the oxygen pressure in said conduit means is limited in a manner dependent upon said predetermined pressure head.

4. The system of claim 3 in which means are provided for assuring a continuous minimum blood pressure comprising the further improvement in said oxygenator.

5. The system of claim 4 comprising the further improvement in which said oxygen line communicates with said gas conduit means upstream from said oxy-

genator.

6. In an extracorporeal oxygenation system in which oxygen and carbon dioxide are transferred across a membranous barrier separating the blood and the oxygen, said oxygenator having a blood inlet, a blood outlet, and an oxygen inlet and outlet; the improvement comprising, in combination: a blood reservoir coupled to said blood outlet downstream therefrom, said blood reservoir being positioned at a higher level than said blood outlet to provide to blood adjacent the membranous barrier a predetermined minimum pressure; and manometer means which comprises a liquid container, open to the atmosphere, being at least partially filled with a liquid; an oxygen supply line coupled to said oxygen inlet, venting conduit means coupled with said oxygen line and communicating with said liquid within said container and having an outlet therein, said liquid having a level that is selected to provide a pressure at said venting conduit means outlet but to permit the venting of the oxygen in order to prevent the pressure of the oxygen from exceeding said minimum pressure of said blood, and further including second manometer means coupled to the blood inlet line, said second manometer means being also operatively connected to said liquid in the container, and responsive to the pressure of the blood in said blood inlet line to automatically adjust the level of said liquid in said container.

* * * * *

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(12) **United States Patent**
Ginsburg, incapacited et al.

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(45) **Date of Patent: Dec. 24, 2002**

(54) **METHOD AND APPARATUS FOR REGIONAL AND WHOLE BODY TEMPERATURE MODIFICATION**

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(52) **U.S. Cl.** **607/106**; 607/113
(58) **Field of Search** 607/96, 105, 106, 607/113; 604/113

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(57) **ABSTRACT**

Methods and apparatus for temperature modification of selected body regions including an induced state of local hypothermia of the brain region for neuroprotection. A heat exchange catheter is provided with heat transfer fins projecting or extending outward from the catheter which may be inserted into selected blood vessels or body regions to transfer heat with blood or fluid in the selected blood vessels or body regions. Another aspect of the invention further provides methods and apparatus for controlling the internal body temperature of a patient. By selectively heating or cooling a portion of the catheter lying within a blood vessel, heat may be transferred to or from blood flowing within the vessel to increase or decrease whole body temperature or the temperature of a target region. Feed back from temperature sensors located within the patient's body allow for control of the heat transfer from the catheter to automatically control the temperature of the patient or of the target region within the patient. The apparatus may include a blood channeling sleeve that directs body fluid over a heat exchanger where the body fluid's temperature is altered, and then is discharged out the distal end of the sleeve to a desired location, for example, cooled blood to the brain for neuroprotection. The catheter may be used alone or in conjunction with other heat exchangers to cool one region of a patient's body while heating another.

73 Claims, 20 Drawing Sheets

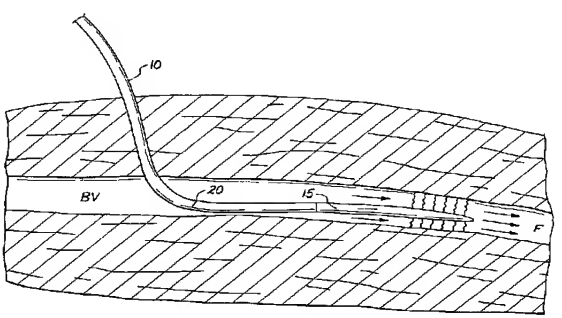

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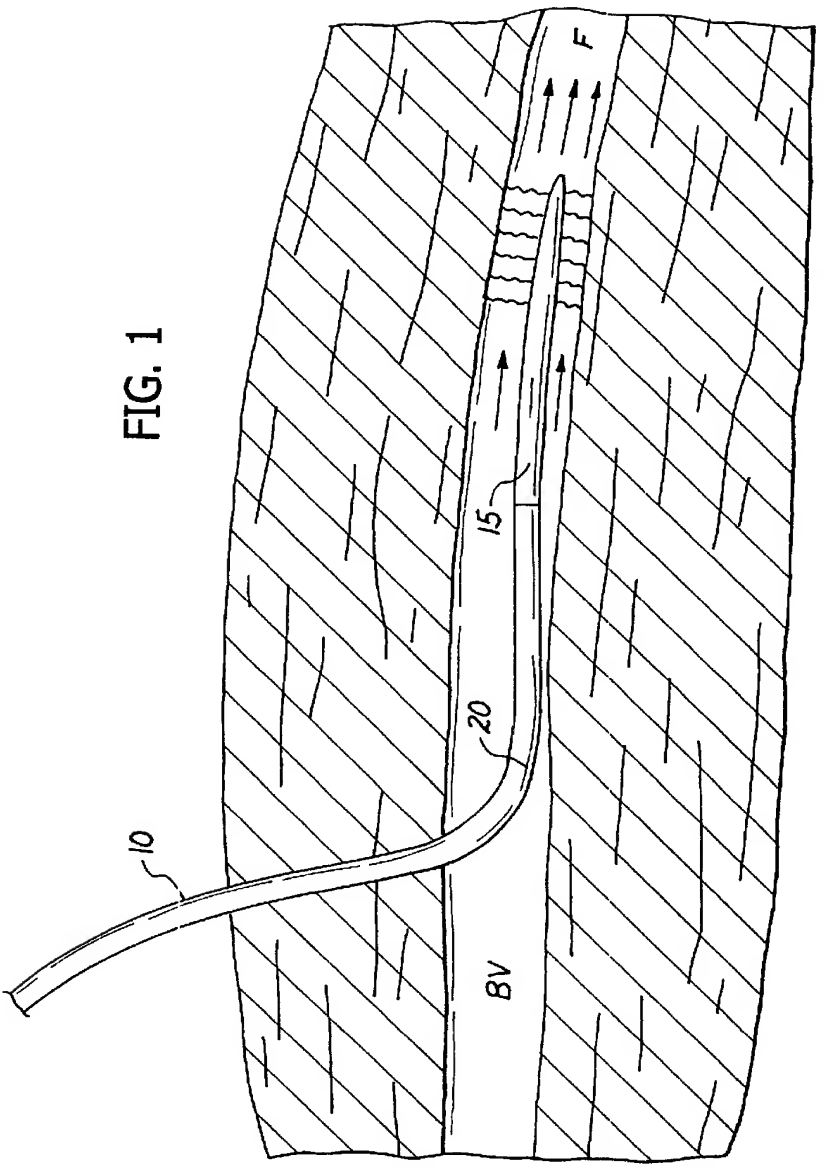
FIG. 1



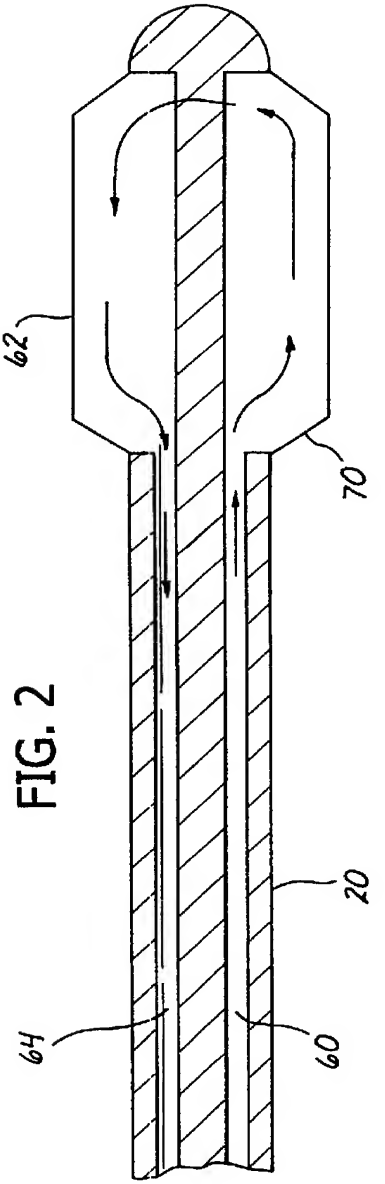
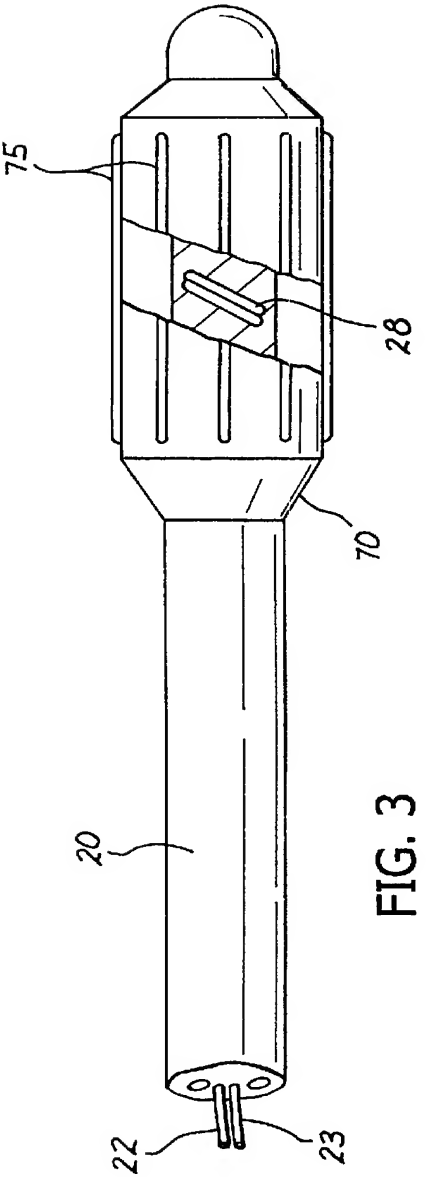


FIG. 2



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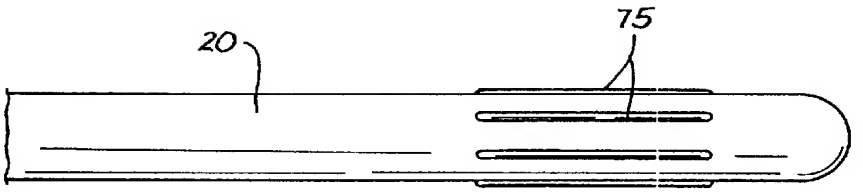


FIG. 4A

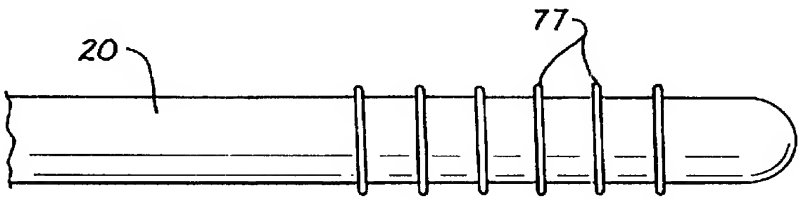


FIG. 4B

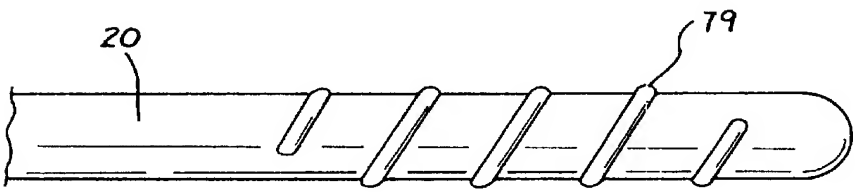


FIG. 4C

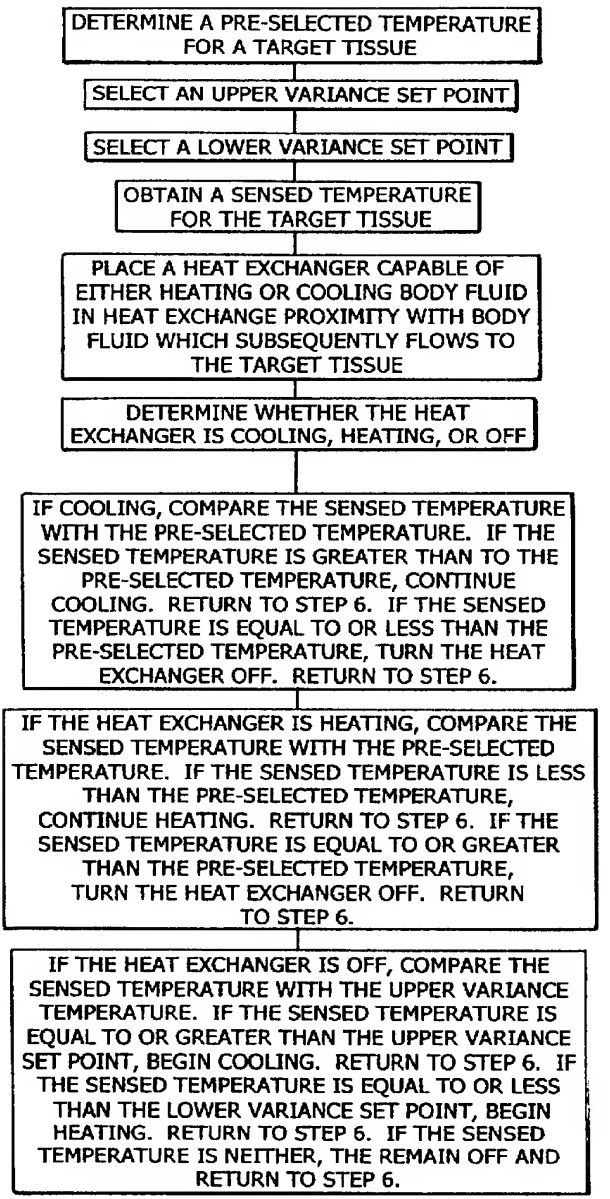
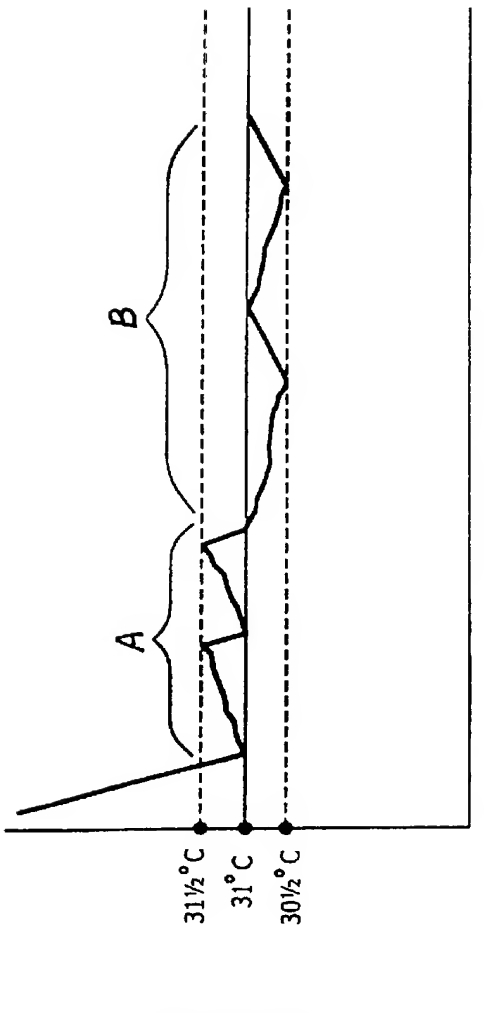

DETERMINE A PRE-SELECTED TEMPERATURE FOR A TARGET TISSUE
SELECT AN UPPER VARIANCE SET POINT
SELECT A LOWER VARIANCE SET POINT
OBTAIN A SENSED TEMPERATURE FOR THE TARGET TISSUE
PLACE A HEAT EXCHANGER CAPABLE OF EITHER HEATING OR COOLING BODY FLUID IN HEAT EXCHANGE PROXIMITY WITH BODY FLUID WHICH SUBSEQUENTLY FLOWS TO THE TARGET TISSUE
DETERMINE WHETHER THE HEAT EXCHANGER IS COOLING, HEATING, OR OFF
IF COOLING, COMPARE THE SENSED TEMPERATURE WITH THE PRE-SELECTED TEMPERATURE. IF THE SENSED TEMPERATURE IS GREATER THAN TO THE PRE-SELECTED TEMPERATURE, CONTINUE COOLING. RETURN TO STEP 6. IF THE SENSED TEMPERATURE IS EQUAL TO OR LESS THAN THE PRE-SELECTED TEMPERATURE, TURN THE HEAT EXCHANGER OFF. RETURN TO STEP 6.
IF THE HEAT EXCHANGER IS HEATING, COMPARE THE SENSED TEMPERATURE WITH THE PRE-SELECTED TEMPERATURE. IF THE SENSED TEMPERATURE IS LESS THAN THE PRE-SELECTED TEMPERATURE, CONTINUE HEATING. RETURN TO STEP 6. IF THE SENSED TEMPERATURE IS EQUAL TO OR GREATER THAN THE PRE-SELECTED TEMPERATURE, TURN THE HEAT EXCHANGER OFF. RETURN TO STEP 6.
IF THE HEAT EXCHANGER IS OFF, COMPARE THE SENSED TEMPERATURE WITH THE UPPER VARIANCE TEMPERATURE. IF THE SENSED TEMPERATURE IS EQUAL TO OR GREATER THAN THE UPPER VARIANCE SET POINT, BEGIN COOLING. RETURN TO STEP 6. IF THE SENSED TEMPERATURE IS EQUAL TO OR LESS THAN THE LOWER VARIANCE SET POINT, BEGIN HEATING. RETURN TO STEP 6. IF THE SENSED TEMPERATURE IS NEITHER, THE REMAIN OFF AND RETURN TO STEP 6.

FIG. 5


A
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31½°C
31°C
30½°C
TEMPERATURE
TIME
31°C = PRE-SELECTED TEMPERATURE
31½°C = UPPER VARIANCE SET POINT
31½°C = LOWER VARIANCE SET POINT

FIG. 6

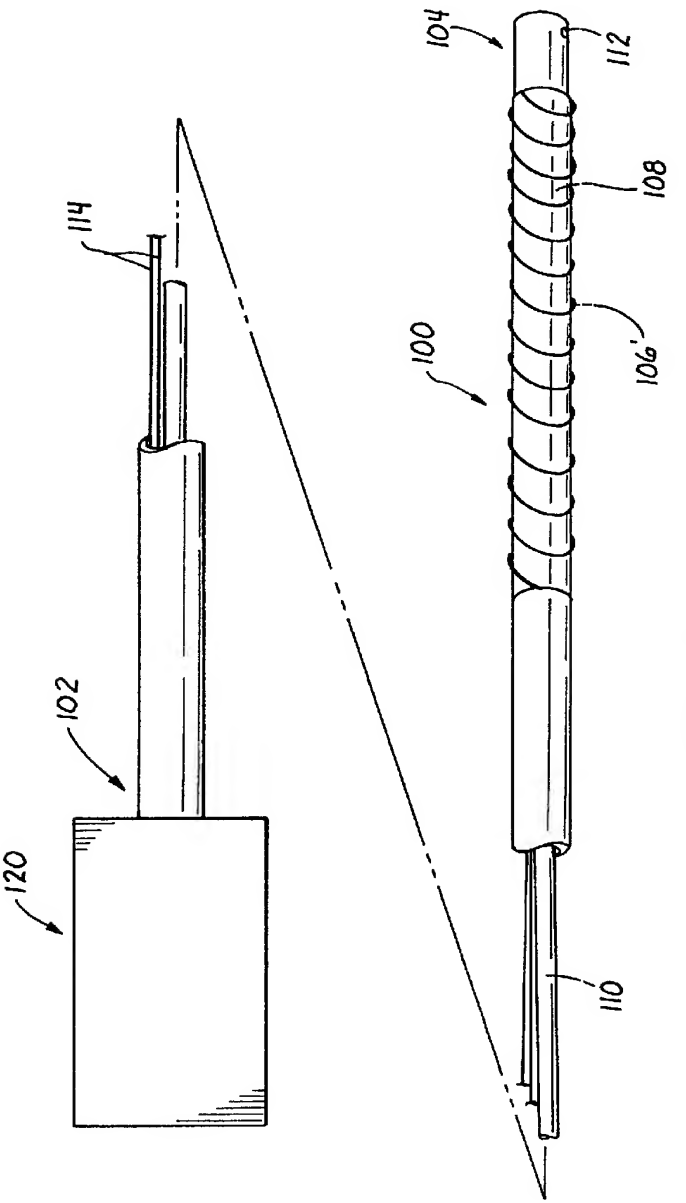


FIG. 7

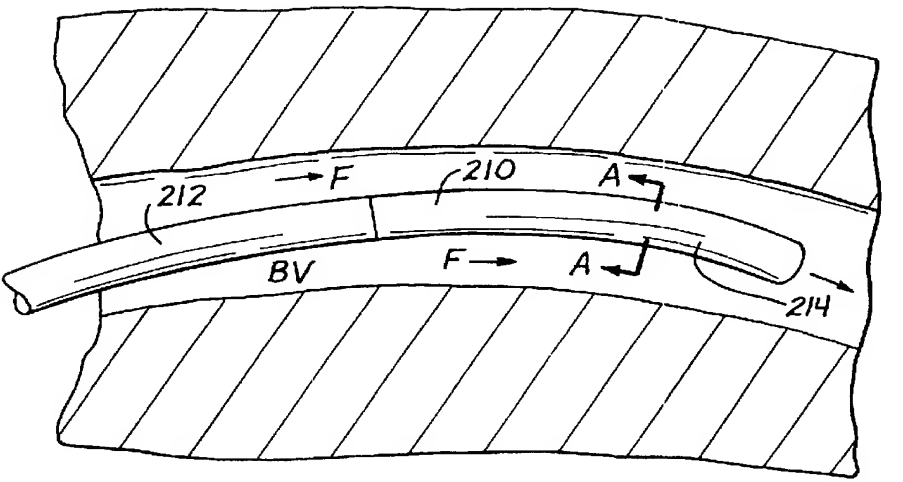


FIG. 8

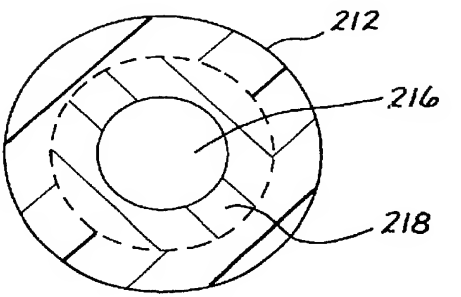
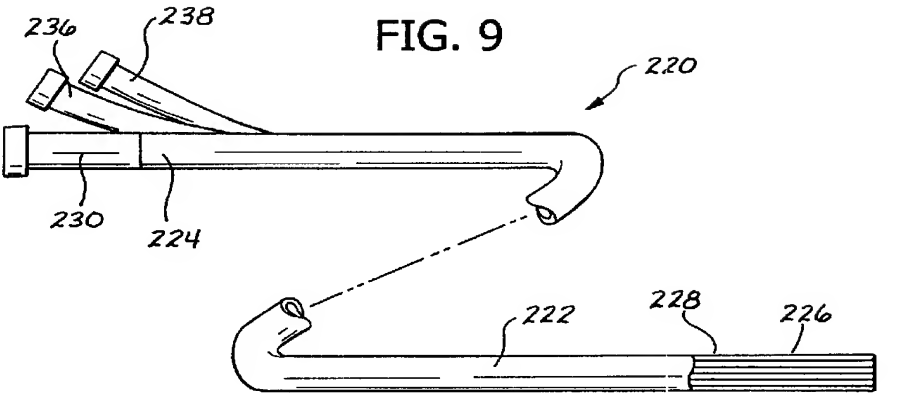


FIG. 8A

FIG. 9



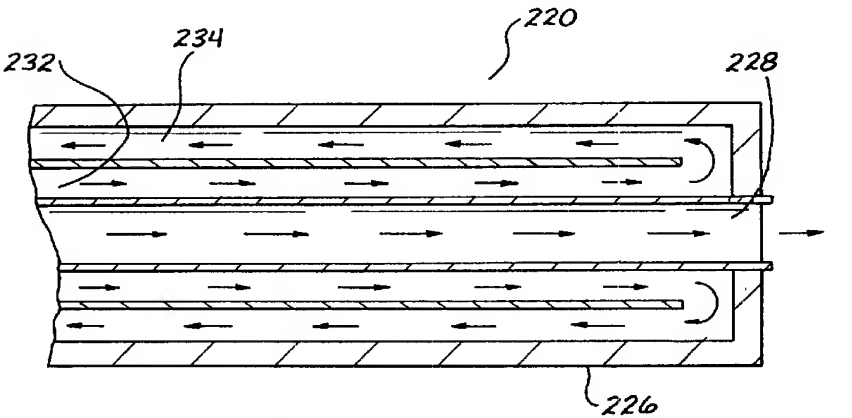


FIG. 10

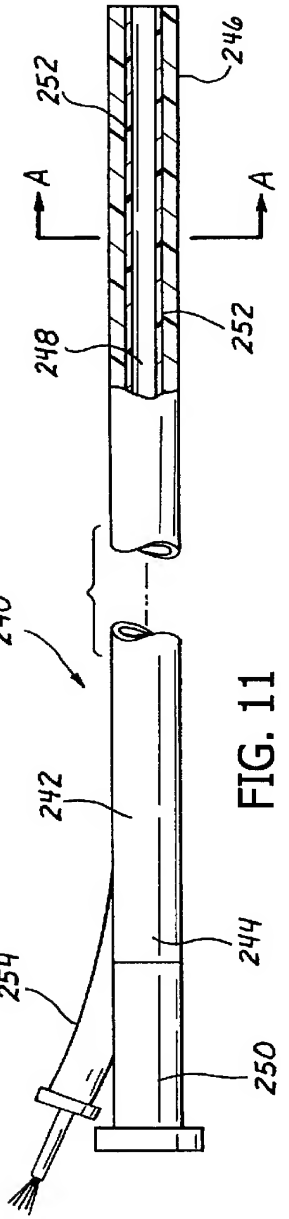


FIG. 11

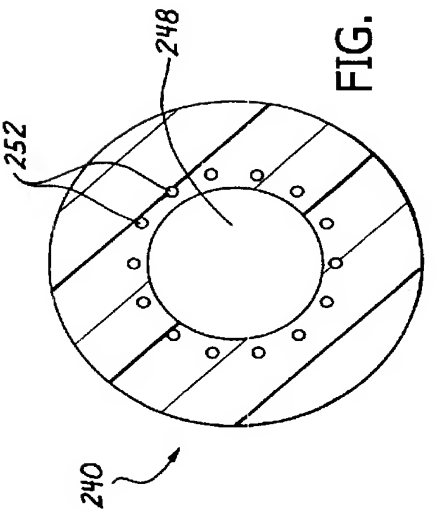


FIG. 11A

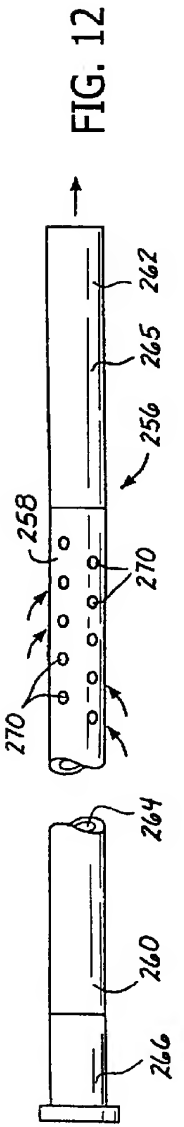


FIG. 12

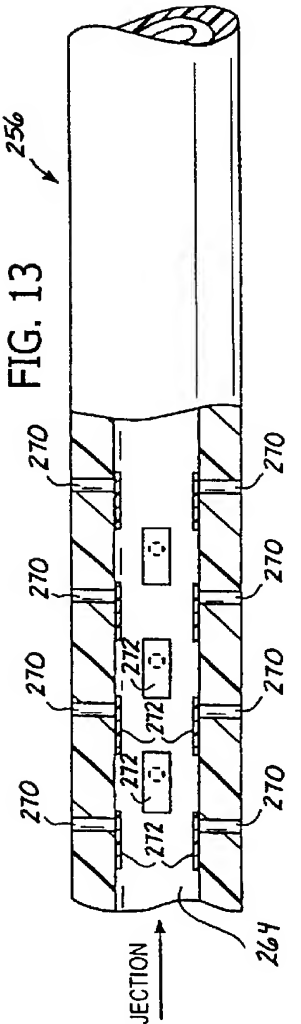


FIG. 13

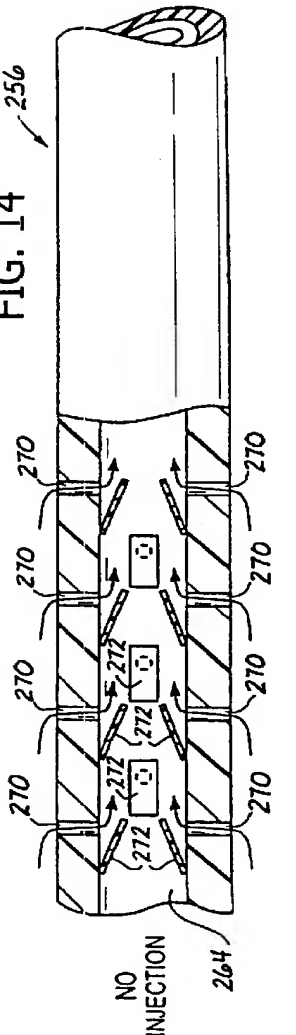


FIG. 14

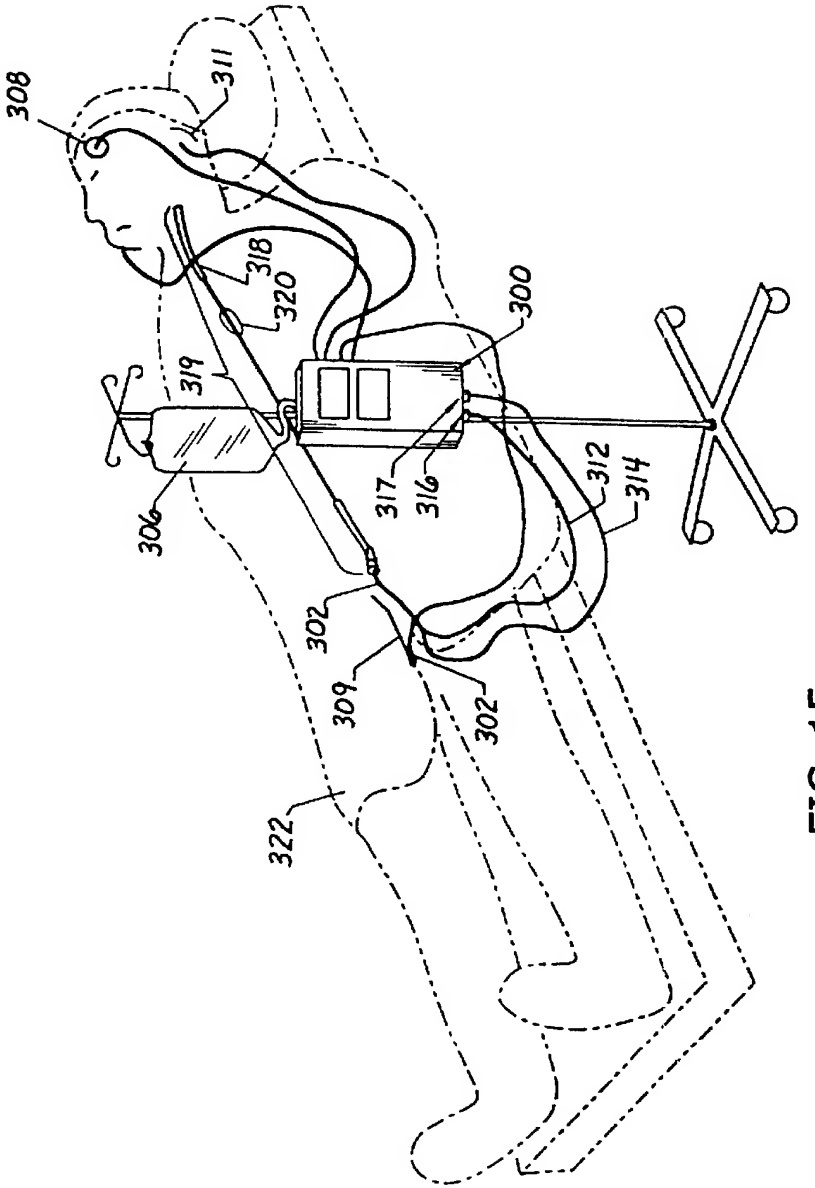


FIG. 15

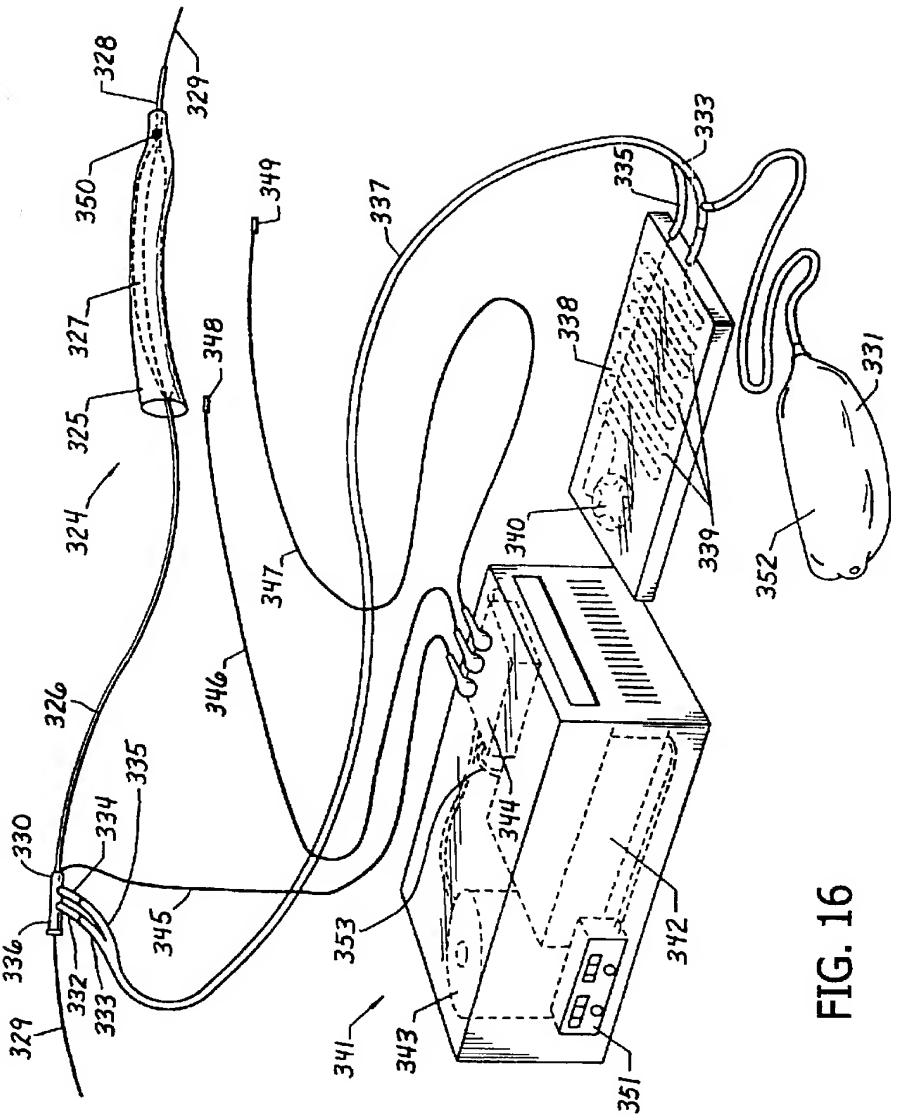

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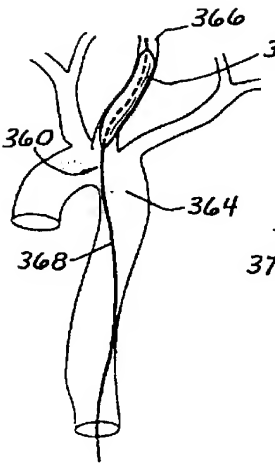
FIG. 16



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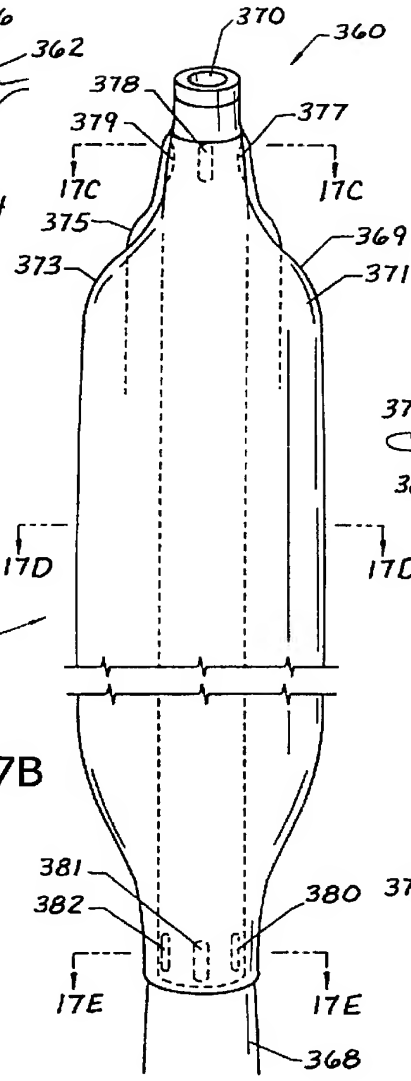


FIG. 17B

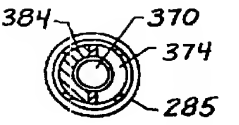


FIG. 17C

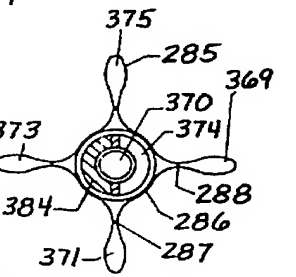


FIG. 17D

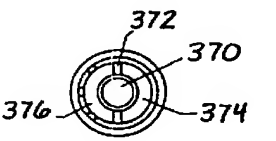
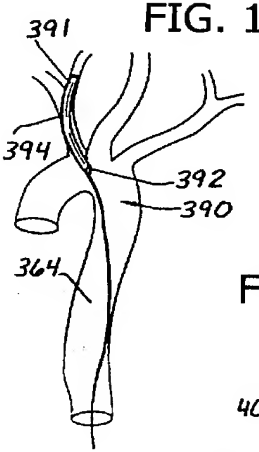
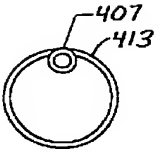


FIG. 17E

FIG. 18A





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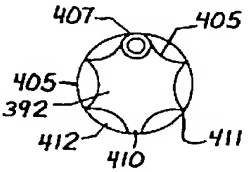
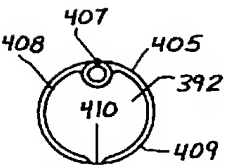


FIG. 18D



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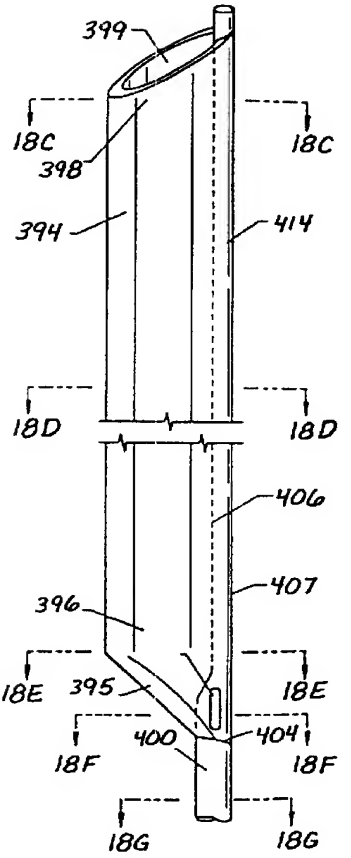

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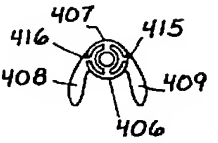

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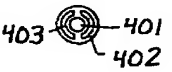

FIG. 18G

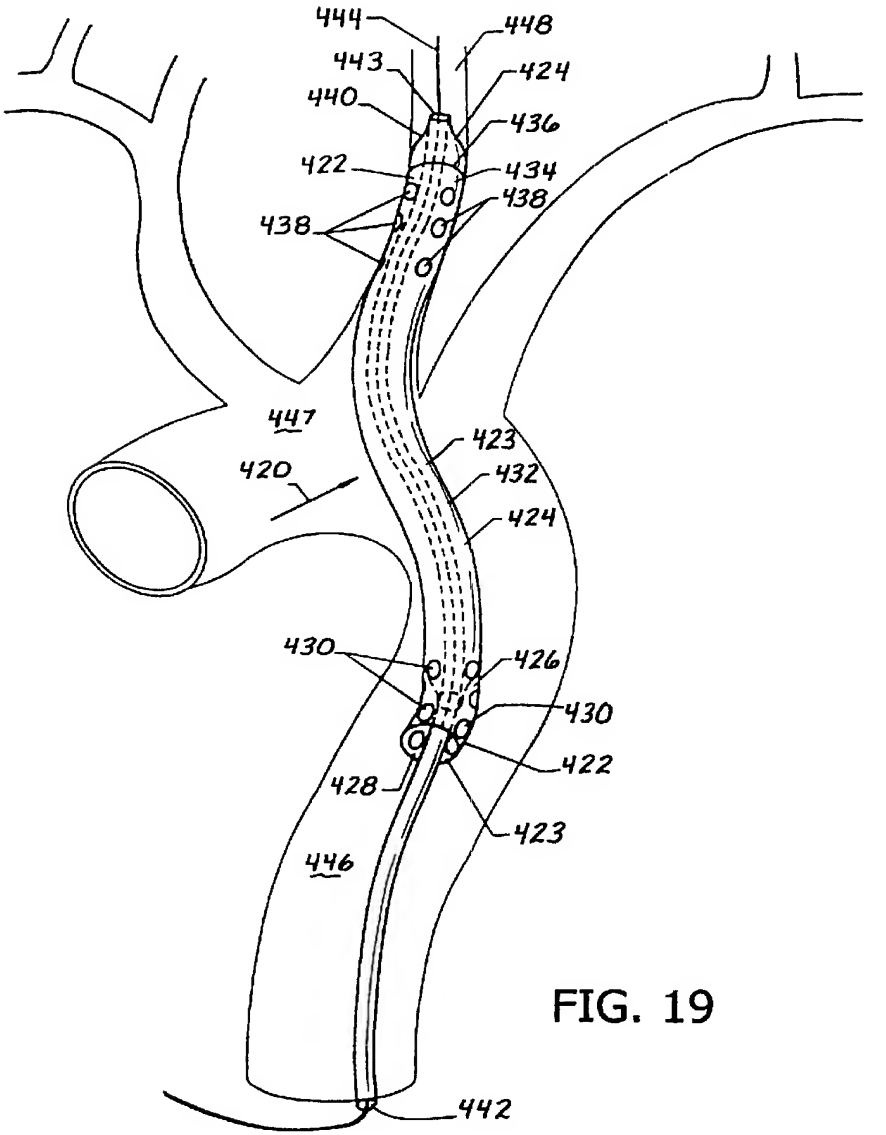
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FIG. 19

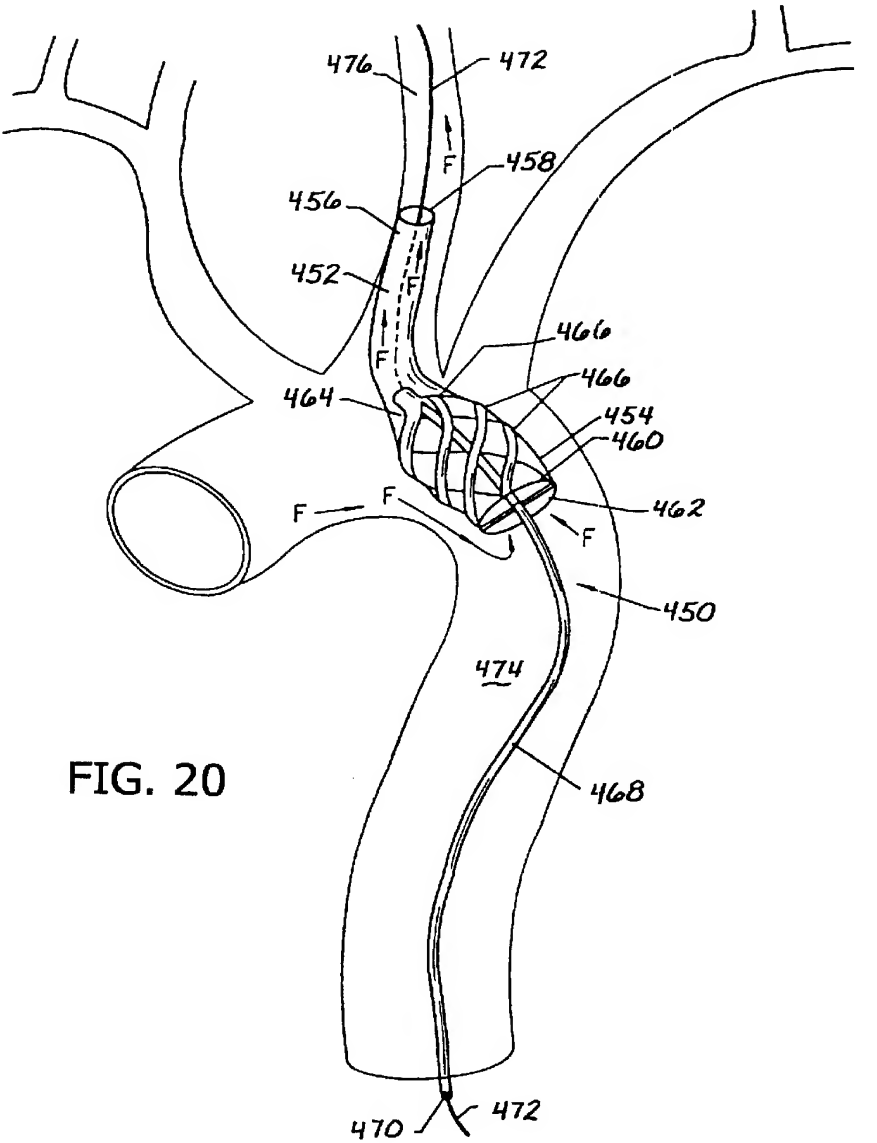
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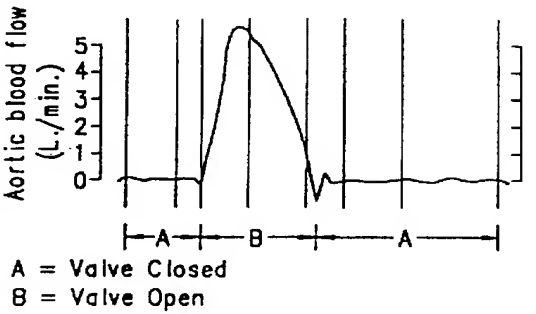
FIG. 20



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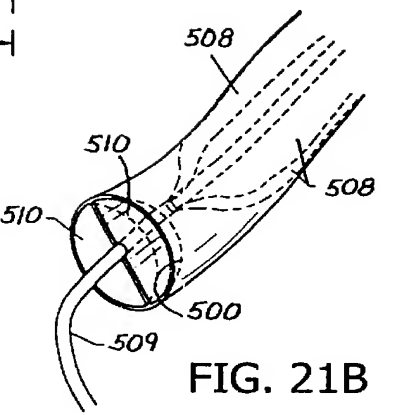
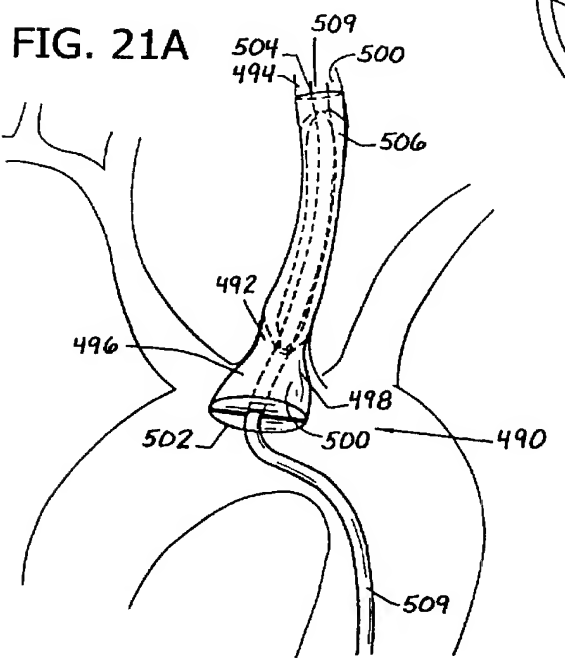


FIG. 21B

FIG. 21A



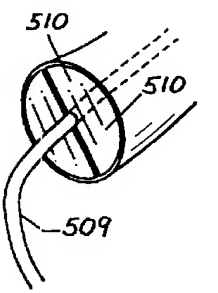


FIG. 21C

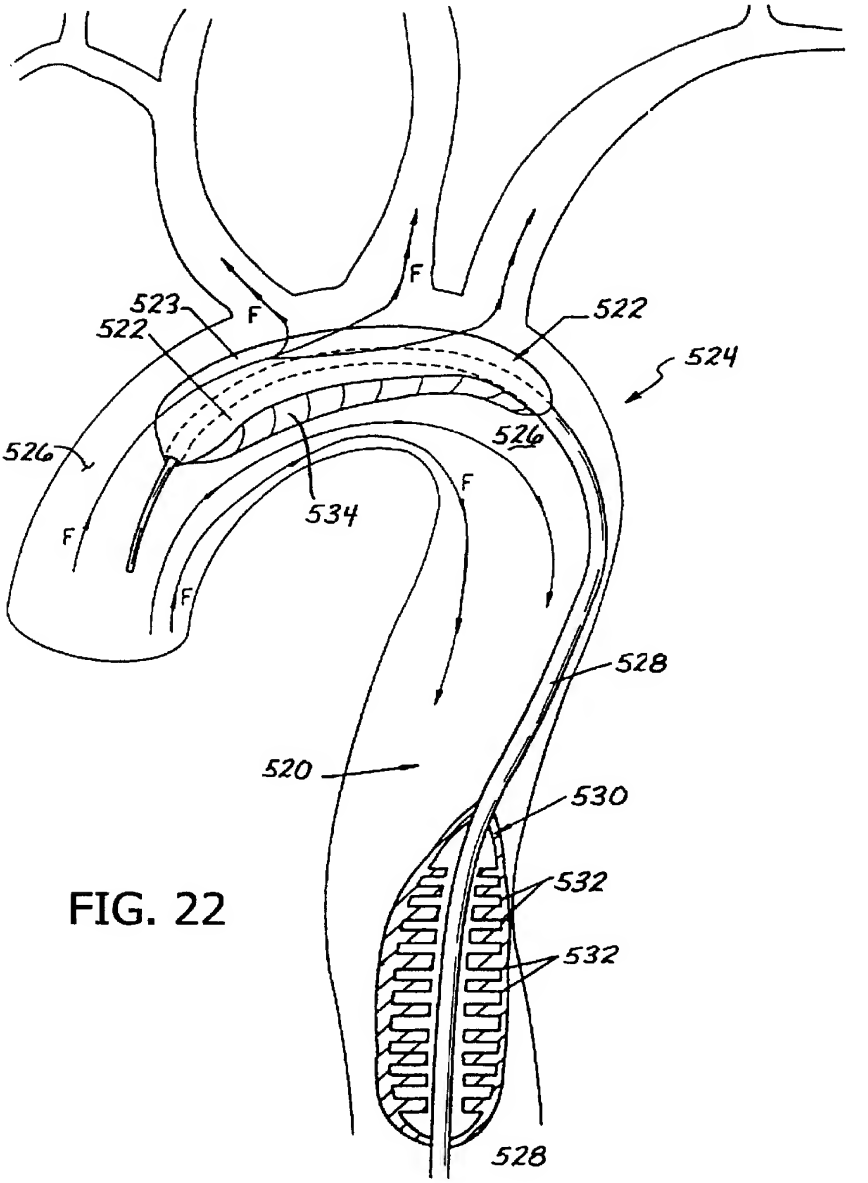
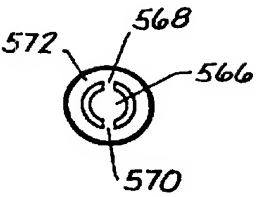


FIG. 22

FIG. 23B



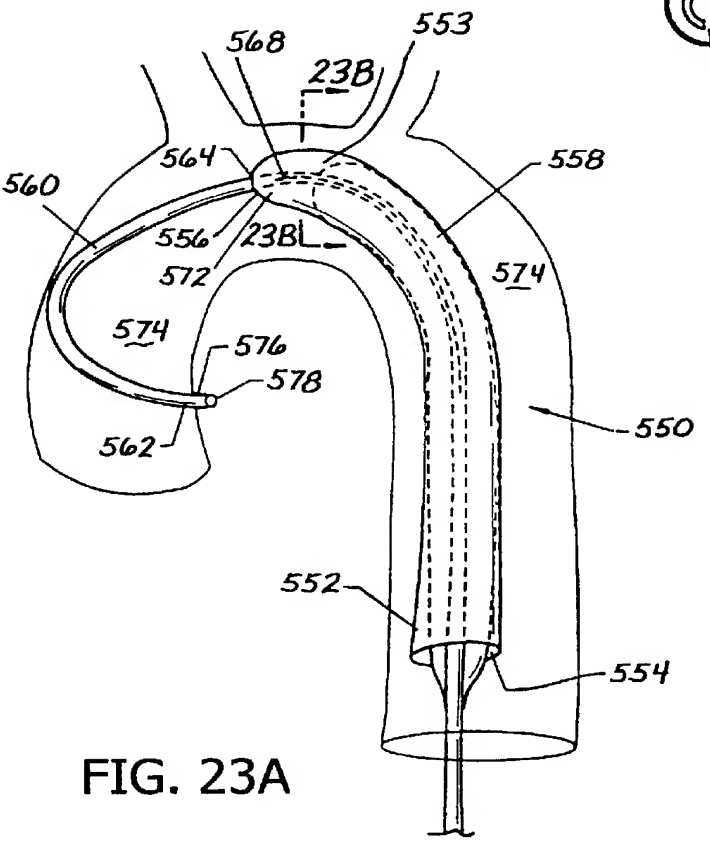


FIG. 23A

FIG. 24A

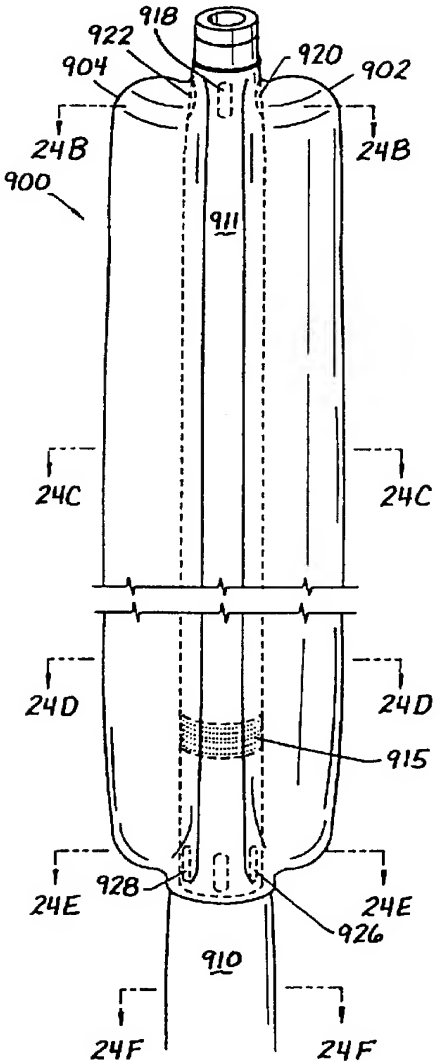


FIG. 24B

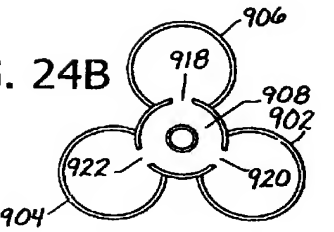


FIG. 24C

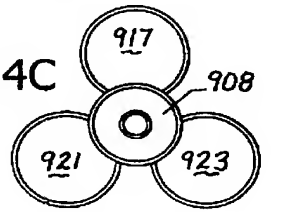


FIG. 24D

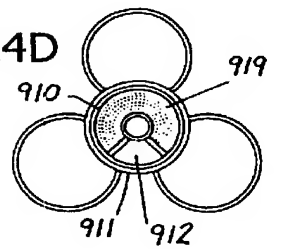
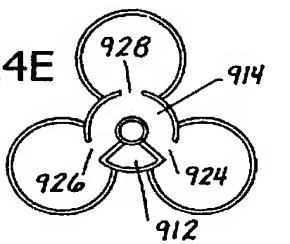


FIG. 24E



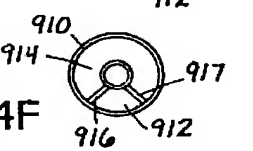


FIG. 24F

METHOD AND APPARATUS FOR REGIONAL AND WHOLE BODY TEMPERATURE MODIFICATION

This is a division of application Ser. No. Ser. No. 09/138,830 filed on Aug. 24, 1998.

FIELD OF THE INVENTION

The present invention generally relates to the selective modification and control of a patient's body temperature, and to the regulation of the temperature of a fluid that is to be delivered to a specific target location within a body structure. More particularly, the invention provides methods and apparatus for treating or inducing hypothermia or hyperthermia by inserting a catheter into a blood vessel of the patient and selectively transferring heat to or from blood flowing through the vessel, and for altering the temperature of a fluid that is to be delivered to the target location while the fluid is within the patient.

The present invention further relates to the selective modification and control of whole body temperature and the temperature of selected target regions of the body such as the brain. More particularly, the invention is directed to methods and apparatus for lowering the temperature of the brain by using heat transfer regions of a heat transfer catheter to cool fluids in contact with, or circulating in, around, or leading to the brain region to provide regional hypothermia and temperature control.

BACKGROUND OF THE INVENTION

Under ordinary circumstances, the thermal regulatory system of the human body maintains a near constant temperature of about 37° C. (98.6° F.). Heat lost to the environment is precisely balanced by internal heat produced within the body.

Hypothermia is a condition of abnormally low body temperature generally characterized by a core body temperature of 35° C. or less, and may be further clinically defined according to its severity. For example, a body core temperature within the range of 32° C. to 35° C. may be described as mild hypothermia, 30° C. to 32° C. as moderate, 24° C. to 30° C. as severe, and a body temperature of less than 24° C. may constitute profound hypothermia. Although the above ranges may provide a useful basis for discussion, they are not absolutes and definitions vary widely as indicated in the medical literature.

Hyperthermia may be defined as a condition of abnormally high body temperature, and may be the result from exposure to a hot environment or surroundings, overexertion, or fever. Body core temperatures may range from 38° C. to 41° C. due to conditions such as fever, and may be substantially higher in cases of exposure and overexertion. Like hypothermia, hyperthermia is a serious condition that can be fatal.

Although both hypothermia and hyperthermia may be harmful and require treatment in some case, in other cases hyperthermia or hypothermia, and particularly hypothermia, may be therapeutic or otherwise advantageous, and therefore may be intentionally induced. For example, periods of cardiac arrest in the setting of myocardial infarction and heart surgery can produce brain damage or other nerve damage. Hypothermia is recognized in the medical community as an accepted neuroprotectant during cardiovascular surgery and therefore a patient is often kept in a state of induced hypothermia during cardiovascular surgery. Likewise, hypothermia is sometimes induced as a neuroprotectant during neurosurgery. Hypothermia may also be beneficial in other situations, for example, for victims of head trauma, spinal trauma, brain attack (also sometimes called stroke), spinal surgery or surgery where blood flow may be interrupted or compromised to the brain or spinal cord such as aneurysm repair, as well as other types of surgery where neuroprotection is desirable.

Neural tissue, that is all tissue of the nervous system such as the brain or spinal cord, is particularly subject to damage by vascular disease processes including, but not limited to ischemic or hemorrhagic stroke, blood deprivation for any reason, including cardiac arrest, intracerebral hemorrhage and head trauma In each of these instances, damage to brain tissue may occur because of ischemia, pressure, edema or other processes resulting in a loss of cerebral function and permanent neurological deficits. Lowering the brain temperature may confer neuroprotection through several mechanisms including the blunting of post-insult elevation of neurotransmitters such as glutamate, reduction of cerebral metabolic rate, moderation of intracellular calcium, prevention of intracellular protein synthesis inhibition, and reduction of free radical formation as well as other enzymatic cascades and even genetic responses. Thus intentionally induced hypothermia may prevent some of the damage to brain or other neurological tissue during surgery or as a result of stroke, intracerebral hemorrhage and trauma.

Treatment of stroke in particular is a possibly therapeutic use of intentionally induced hypothermia. Stroke (sometimes called brain attack) is a severely debilitating and complex disease that results from the blockage (ischemic stroke) or rupture (hemorrhagic stroke) of a blood vessel within or leading to the brain region. During a stroke, brain cells are damaged either by a lack of oxygen or by increased pressure. These events can eventually result in death and necrosis of brain tissue. In general, at least one goal in the therapeutic intervention for stroke is to preserve the function of as much brain tissue as possible. However, current medical treatment for stroke is largely supportive in nature. Newer treatments, for example clot-dissolving drugs, are available but may be only suitable for treatment of ischemic strokes and must generally be used shortly (within several hours) of the initial stroke symptoms to avoid side effects related to bleeding within the brain. In practice, it has been difficult to treat strokes within this time window since patients often do not arrive at a medical facility until several hours after the onset of a stroke. As a result, most strokes are not aggressively treated with medical therapy. A treatment to prolong this time window, and to protect brain cells from death, would have a profound impact on patient care.

Experimental studies of ischemia have shown reduction in infarcted brain tissue volume in animals treated with hypothermia during or shortly after a stroke or ischemic insult. It is therefore believed that the application of hypothermia to a patient who is suffering or has recently suffered a stroke may be beneficial.

Despite the acceptance of hypothermia as a neuroprotectant, it has not been widely used outside of the surgical setting. Additionally, most current practices attempt to provide hypothermia to the brain by inducing whole body hypothermia through systemic treatment. However, whole body hypothermia presents numerous difficulties and is cumbersome to implement in a patient who is not under general anesthesia. Lowering the systemic temperature of a patient not only takes a significant amount of time, but also subjects the patient to deleterious effects of hypothermia including cardiac arrhythmias, coagulation problems, increased susceptibility to infections, and problems of discomfort such as profound shivering.

Control of the body's temperature, for example, to maintain normothermia (usually 37° C.), is often desirable. For example, in a patient under general anesthesia, the body's normal temperature regulating mechanisms may not be fully functioning, and the anesthesiologist may be required to artificially control the patient's body temperature. Similarly, a patient may lose an extraordinary amount of heat to the environment, for example, during major surgery, and the patient's unaided body may not be able to generate sufficient heat to compensate for the heat lost. A device and method for controlling body temperature, for example by adding heat to maintain normothermia, would be desirable.

Particularly in the surgical setting, it has sometimes been the case that blood or other fluid was heated or cooled outside a patient's body and introduced into the body to heat or cool the body or some target location within the body. However, heating or cooling fluids outside of the patient may be cumbersome and require elaborate equipment. For example, in surgery, the temperature of a patient may be controlled by a bypass machine where a significant amount of the patient's blood is removed, heated or cooled outside the body in a by-pass machine, and reintroduced to the patient's blood stream. One particular application of this procedure is whole body hypothermia sometimes induced during heart surgery. Other examples include hypothermia induced during neurosurgery or aortic or other vascular surgery.

The use of an external method for inducing hypothermia, such as a bypass machine, is an extremely invasive procedure that subjects vast quantities of the patients' blood to pumping for an extended length of time. External pumping of blood may be harmful to the blood, and continued pumping of blood into a patient for extensive periods of time, for example, more than one or two hours, is generally avoided. Additionally, such a procedure may require systemic treatment of the patient, for example, with heparin to prevent clotting which may present other undesirable consequences in a stroke victim.

Means of imparting heat to the blood of a patient, or removing heat from the patient, which do not require external pumping have been proposed. For example, one particular catheter structure which has been developed to treat patients suffering from either hypothermia or hyperthermia is described in U.S. Pat. No. 5,486,208, to Ginsburg, the complete disclosure of which is herein incorporated by reference. That patent issued from one of the applications from which this application claims priority. A catheter disclosed in that patent was inserted into a blood vessel and a portion of the catheter heated or cooled, transferring heat to the patient's blood and thereby affecting the overall body temperature of the patient. However, while such devices and methods may avoid the problems associated with external pumping of blood, they do not eliminate the difficulties that arise when the entire body is subjected to hypothermia.

There have been attempts to achieve regional cerebral hypothermia, for example by placing the head in a cooled helmet or shroud, or even injecting a cold solution into the head region. Attempts to achieve brain cooling by directly cooling the surface of the head have proven impractical or ineffective because of factors such as the insulating qualities of the skull, which make it difficult to effectively lower brain core temperature, and the blood flow that may fail to provide sufficient heat transfer circulation to the brain itself when the surface of the head is cooled. Patients, especially patients not under general anesthesia, may also find it difficult to tolerate immersion or direct exposure of the head to a cold solution or cooling surface.

An apparatus to facilitate transfer of heat to or from a target location by means of internally applied heating or cooling would be advantageous. It has been known in the art to impart heat by direct contact with specific tissue by means of a balloon catheter. For example, in U.S. Pat. No. 5,019,075 to Spears, a heated balloon was described to apply heat directly from the surface of the balloon to the wall of an artery dilated during percutaneous transluminal coronary angioplasty (PTCA) to fuse together disrupted tissue. This device, however, operated by direct contact between the vessel wall in question and a greatly heated balloon surface.

Balloons capable of acting as ongoing heat transfer balloons by the continual flow of heat transfer medium through the balloon have also been shown. For example, in U.S. Pat. No. 5,624,392 to Saab, a concentric inflow and outflow lumen each terminate within the heat transfer balloon so that a continual flow of heat transfer liquid can be maintained within the balloon for controlled heat transfer to the adjacent tissue.

U.S. Pat. No. 5,269,758 to Taheri, discloses a balloon in which heated fluid such as heated saline solution is circulated through a balloon that pulses. The heat from the heat transfer liquid may then be imparted to the blood as it flows past the balloon to treat hypothermia in a patient. The flow of the affected blood is not otherwise generally directed nor is the temperature of a target region disclosed to be altered by the heated balloon of Tahari.

The configuration of balloons to provide channels for the flow of blood from the proximal side to the distal side of a balloon blocking a blood vessel, such as a balloon used for PTCA has also been shown. For example, such an autoperfusion balloon angioplasty catheter is shown in U.S. Pat. No. 4,581,017 to Sahota, and the multi-lumen balloon shown in U.S. Pat. No 5,342,301 to Saab as discussed for use in angioplasty discloses a multi-lumen balloon catheter configured to allow blood to perfuse from the proximal side to the distal side of a balloon angioplasty catheter when the balloon is inflated to apply angioplastic pressure against the blood vessel walls and otherwise fully obstruct blood passage.

It would be desirable to devise an apparatus capable of heating or cooling liquid such as blood within the body and directing that liquid after it is heated or cooled, to a target location. It would be particularly advantageous if a device could be devised where the liquid could be directed to a desired location using only the patient's own heart as a pump. It would also be particularly advantageous if a method could be devised for directing heated or cooled blood to a target region of a patient's body for a sufficient length of time to affect the temperature of that target region.

A method of treating a patient to protect tissue, and particularly neural tissue, by inducing hypothermia is desirable. Protecting particular target tissue by inducing hypothermia in that tissue by means of in situ cooling of body fluid directed to that tissue would be particularly advantageous.

It would also be desirable to provide a system to control such a device to perform the method of treatment in a simple and predictable manner. It would be particularly desirable if such a system could control the device in conjunction with feedback data from a patient to control the device to predictably and selectively affect the temperature of a target region in the patient.

SUMMARY OF THE INVENTION

The present invention provides heat exchange catheter devices which generally comprise an elongate flexible cath-

eter having a heat exchanger which is operative to exchange heat between blood or other body fluid which flows in heat exchanging proximity thereto. Also, the present invention provides methods for utilizing such heat exchange catheter devices to selectively heat or cool a particular region (e.g., the brain, a selected portion of the brain, the spinal cord, an organ, an intra-abdominal organ, the spleen, the liver, the heart, a portion of the heart, a lung, a kidney, a muscle, a tumor, a site where trauma has occurred, a site where hemorrhage has occurred, etc.) of the body of a mammalian patient.

In accordance with the devices of the present invention; there is provided a heat exchange catheter device which may generally comprise: i) an elongate catheter having a proximal end and a distal end, the entire length of said flexible catheter being defined as the distance from its proximal end to its distal end; ii) at least one fluid lumen through which a thermal exchange fluid may be circulated, and, iii) a heat exchanger with heat exchange fins located at a first location on the catheter, and a working lumen extending from outside the patient through at least part of the catheter that is inserted into the patient. The heat exchanger is operative to exchange heat between blood which flows in heat exchanging proximity to the heat exchanger and a thermal exchange fluid which is circulated through the catheter. The "first location" at which the heat exchanger is located may constitute less than the entire length of the catheter, and is typically at or near the distal end of the catheter. The heat exchanger may specifically comprise a balloon or other structure through which the thermal exchange fluid may circulate, and the heat exchange fins may be a plurality of lobes of the balloon or may be surface area increasing projections (e.g., outwardly extending protuberances, ribs, etc.) to enhance the efficiency with which heat exchange occurs. Also, in some embodiments of the catheter device, a body fluid channeling sleeve may be formed about the portion of the catheter whereupon the heat exchanger is located (and may extend some distance proximal to the heat exchanger) to channel a flow of blood or other body fluid in heat exchanging proximity to the heat exchanger. Such body fluid channeling sleeve may thus be utilized to channel available body fluid (e.g., blood) form one anatomical conduit (e.g., the descending aorta) in which the proximal end of the sleeve is located, into a second anatomical conduit (e.g., a carotid artery) in which the distal end of the sleeve is located. The sleeve may be sized and configured to form a shoulder that forms a snug seal between the outside of the sleeve and the second anatomical conduit.

The catheter device may further be provided in combination with a device (such as a guide wire, or embolectomy catheter) or medicament (such as a thrombolytic agent or barbiturate) for insertion through the working lumen.

The catheter device of the invention may also comprise a curved heat exchange balloon with an insulated side and a thermoconductive side, and may be placed in the anatomy such that blood flowing to the brain flows past the thermoconductive side and blood flowing to the rest of the body flows past the insulated side.

Finally, another aspect of the invention is the catheter device in combination with a control system that senses body conditions such as temperature and controls the catheter in response to the body conditions sensed, such as turning off the heat exchanger when the patient's target region reaches a pre-selected temperature, or reactivating the heat exchanger when the temperature strays from that pre-selected temperature.

In accordance with the methods of the present invention, there is provided a procedure for modulating or changing the temperature of a selected region of the body of a mammalian patient. Such method comprises the steps of:

a. inserting a catheter device of the foregoing character into an anatomical conduit of the patient's body through which a body fluid flows to the selected region of the patient's body, and positioning the catheter such that body fluid flowing through the anatomical conduit to the selected region will pass in heat exchanging proximity to the heat exchanger before reaching said selected region; and,

b. utilizing the heat exchanger of the catheter device to change the temperature of body fluid which passes in heat exchanging proximity to the heat exchanger, such that said body fluid will subsequently change the temperature of said selected region of the patient's body.

Still further in accordance with the methods of the present invention, the catheter device may be positioned in a blood vessel which leads to the brain (e.g., the right common carotid artery, left common carotid artery, innominate artery, right internal carotid artery, left internal carotid artery, etc.) and used to cool the brain or a portion thereof to deter neural damage following a stroke or other insult (e.g., period of ischemia, period of hypoxia, hemorrhage, trauma, etc.).

Still further in accordance with the methods of the present invention, two or more catheter devices of the foregoing character may be simultaneously positioned at different sites within the patient's body so as to selectively heat or cool body fluid (e.g., blood) which is flowing to the selected body region, and to subsequently return such body fluid to or close to its original temperature as it flows from the selected body region. In this regard, one heat exchange catheter device may be positioned in an artery which perfuses the brain to cause cooling of the brain following a stroke or other insult, and a second catheter may be positioned in the inferior vena cava or other suitable vein to re-Warm blood after it circulates through the brain, or to generally add heat to blood going to the trunk of a patient's body to maintain normothermia in the body at locations other than the cooled region.

Another aspect of the invention provides a method of controlling the heat exchange with the body fluid such that a predetermined temperature may be established at a target tissue, and may be maintained. As an additional aspect, a predetermined temperature may be established for the target tissue, for example a particular hypothermic temperature for the brain, and another temperature may be selected for another region, for example the core body temperature being normothermic, and two catheters may be simultaneously controlled to maintain both pre-selected temperatures.

Further aspects and details of the present invention will become apparent to those of skill in the relevant art upon reading and understanding of the detailed description of preferred embodiments set forth here below. Each of the embodiments disclosed below may be considered individually or in combination with any of the other variations and aspects of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts a catheter according to the present invention inserted percutaneously into a blood vessel of a patient.

FIG. 2 depicts a catheter in which a heated or cooled fluid flows through a balloon, which provides for an increased surface area near the distal end of the catheter.

FIG. 3 depicts a catheter having a resistance heating element at its distal end and a balloon having longitudinal ribs to further increase the heat transfer surface area.

FIG. 4A depicts a catheter having longitudinal fins at the distal end of the catheter body.

FIG. 4B depicts a catheter having radial ribs at the distal end of the catheter body.

FIG. 4C depicts a catheter having a spiral fin to increase the heat transfer area at the distal end of the catheter.

FIG. 5 is a flow chart describing the control scheme of the invention.

FIG. 6 is a diagrammatic representation of the temperature of target tissue under the influence of the control system of FIG. 5.

FIG. 7 illustrates a preferred catheter for the selective heating and cooling of patient blood flow employing a wire coil resistance heater and a metal foil cooling element.

FIG. 8 depicts a distal end of a catheter according to the present invention which is inserted into a vessel of a patient.

FIG. 8A is a cross-sectional side view of a catheter shown in FIG. 8 taken along lines A—A and depicting a temperature altering region.

FIG. 9 is a side view of an exemplary catheter for heating or cooling a fluid passing through an internal lumen according to the invention.

FIG. 10 is a more detailed view of a distal end of a catheter similarly shown in FIG. 9.

FIG. 11 is a side view of an alternative catheter for heating a fluid passing through an internal lumen according to the invention.

FIG. 11A is a side view of the catheter of FIG. 11 taken along lines A—A.

FIG. 12 is a side view of another alternative embodiment of a catheter for heating or cooling a fluid passing through an internal lumen and having a plurality of perfusion orifices for allowing body fluids to enter into the internal lumen according to the invention.

FIG. 13 is a cutaway side view of a portion of a catheter similarly illustrated in FIG. 12 showing a plurality of flaps which are closed to prevent body fluids from entering into the internal lumen when a liquid is externally injected into the lumen.

FIG. 14 illustrates a catheter similarly illustrated in FIG. 13 showing the flaps opening to allow body fluids to enter into the internal lumen when no fluids are externally injected into the lumen.

FIG. 15 is a perspective view of a heat transfer catheter system connected to a patient that may include monitoring devices, a controller, and a thermal catheter with multiple heat transfer portions.

FIG. 16 is a simplified perspective view of a heat transfer catheter system with a controller, disposable components, reusable components, a heat exchange balloon catheter and various sensors.

FIG. 17A is a simplified perspective view of a variation of the heat transfer catheter of the invention in place within the left common carotid artery.

FIG. 17B is a simplified perspective view of the distal portion of a finned thermal balloon catheter in accordance with one aspect of the invention having a balloon heat transfer portion for supporting the circulation of heat transfer fluid.

FIG. 17C is a simplified cross-sectional view of the catheter illustrated in FIG. 17B taken along line C—C.

FIG. 17D is a simplified cross-sectional view of the catheter illustrated in FIG. 17B taken along line D—D.

FIG. 17E is a simplified cross-sectional view of the catheter illustrated in FIG. 17B taken along line E—E.

FIG. 18A is a simplified perspective view of a variation of the heat transfer catheter of the invention in place within the aorta, the innominate artery, and the right common carotid artery.

FIG. 18B is a perspective view in greater detail of the heat transfer catheter of FIG. 18A formed with a blood channeling sleeve defined by openings that may be in communication with a fluid-containing body region.

FIG. 18C is a simplified cross-sectional view of the catheter illustrated in FIG. 18B taken along line C—C.

FIG. 18D is a simplified cross-sectional view of the catheter illustrated in FIG. 18B taken along line D—D.

FIG. 18E is a simplified cross-sectional view of the catheter illustrated in FIG. 18B taken along line E—E.

FIG. 18F is a simplified cross-sectional view of the catheter illustrated in FIG. 18B taken along line F—F.

FIG. 18G is a simplified cross-sectional view of the catheter illustrated in FIG. 18B taken along line G—G.

FIG. 19 is a simplified illustration of a heat transfer catheter shown in the aorta and having a blood channeling sleeve with a proximal opening in the descending aorta and a distal opening in the left common carotid artery.

FIG. 20 is a simplified perspective view of a variation of the heat transfer catheter of the invention formed with an elongated shaft and a tapered catheter body with spiral shaped fins, and located in the aorta and left common carotid artery.

FIG. 21A is a simplified perspective view of another variation of the thermal catheter formed with an occlusive shoulder and valve assembly.

FIG. 21B illustrates a proximal or distal sleeve valve in a closed position for a thermal catheter of the type shown in FIG. 21A.

FIG. 21C illustrates a proximal or distal sleeve valve in an open position for a thermal catheter of the type shown in FIG. 21A.

FIG. 21D provides a graphical representation of a heartbeat cycle with aortic blood flow measured against the synchronous opening and closing of a sleeve valve similarly shown in FIGS. 21A–C.

FIG. 22 is a heat transfer catheter with a plurality of heat transfer regions that may be configured for placement in the aortic region.

FIG. 23A is a simplified perspective drawing of a version of the heat exchange catheter of the invention having an entry for cooled blood into a central lumen, the distal end of the central lumen inserted into the coronary ostium.

FIG. 23B is a cross-sectional view of FIG. 29 taken along lines B—B.

FIG. 24A is a simplified perspective view of a finned thermal balloon catheter, the fins being inflatable balloon lobes.

FIG. 24B is a simplified cross-sectional view taken along the line B—B in FIG. 24A.

FIG. 24C is a simplified cross-sectional view taken along the line C—C in FIG. 24A.

FIG. 24D is a simplified cross-sectional view taken along the line D—D in FIG. 24A.

FIG. 24E is a simplified cross-sectional view taken along the line E—E in FIG. 24A.

FIG. 24F is a simplified cross-sectional view taken along the line F—F in FIG. 24A.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides methods and apparatus for selectively controlling regional and whole body temperature

by warming or cooling a body fluid such as blood in situ and directing the warmed or cooled body fluid to a desired location. According to the present invention, a catheter having a heat exchanger which may be, for example, a balloon with fins, is inserted into a fluid containing portion of the patients body, for example, a blood vessel. A blood channeling sleeve is mounted over the heat exchanger and is open at both its proximal end (closest to the insertion point) and its distal end (farthest along the catheter from the insertion point). The distal end of the sleeve is placed so that fluid such as blood that enters the proximal end of the sleeve flows in heat transfer proximity past the heat exchanger. Heat exchange proximity requires sufficient proximity for effective heat exchange to occur and depends on such factors as the chemical and physical make-up of the blood, the rate of flow past the heat exchange surface, the pattern of blood flow past the heat exchanger, (laminar flow, turbulent flow, and the like), the difference in temperature between the heat exchange surface and the blood, the material of which the heat exchange surface is made, and the proximity between the heat exchange surface and the blood. Fluid exits the distal end of the sleeve so that the heated or cooled blood is discharged in a desired location, for example upstream of target tissue such as the brain. By continuing to heat or cool fluid flowing to the target tissue for a sufficient length of time, the temperature of the target tissue is altered.

Likewise, when inducing hypothermia or hyperthermia, the invention provides for heating or cooling the target tissue to the desired temperature and maintaining that temperature by controlling the heat exchange catheter. Similarly, different regions may be controllably maintained at temperatures different from each other by controlling different heat exchange catheters at different locations with the patient's body. Additionally, the temperature of the target tissue may be maintained at a desired temperature, for example, mildly hypothermic, while the core temperature of the body may be monitored and maintained at a different temperature, for example, normothermic (37° C.) or nearly normothermic, by use of a separate heat exchange catheter or an additional heat exchange region located on the same heat exchange catheter.

FIG. **1** depicts a distal portion **15** of a heat exchange catheter **10**. The catheter may be inserted through the patient's skin into a blood vessel BV. Blood flow through the vessel is indicated in FIG. **1** by a set of flow arrows F. The catheter may be inserted into a relatively large blood vessel, e.g., a femoral artery or vein, a jugular vein, since these vessels provide numerous advantages in that they are readily accessible, provide safe and convenient insertion sites, and have relatively large volumes of blood flowing through them. In general, large blood flow rates facilitate quicker heat transfer into or out of the patient. For example, the jugular vein may have a diameter of about 22 French, or a bit more than 7 millimeters (1 French=1 mm/π). A catheter suitable for insertion into a vessel of this size can be made quite large relative to catheters intended for insertion into other regions of the vascular system. Atherectomy or balloon angioplasty catheters are sometimes used to clear blockages from the coronary artery and similar vessels. These catheters commonly have external diameters in the range between 2 and 8 French. However, a catheter formed in accordance with this aspect of the invention may have an external diameter of about 10 French or more, although this dimension may obviously be varied a great deal without departing from the basic principles of the invention.

The catheter may be small enough so that the puncture site can be entered using the percutaneous Seldinger technique, a technique well known to medical practitioners. To avoid vessel trauma, the catheter will usually be less than 12 French in diameter upon insertion. Once in the vessel however, the distal or working end of the catheter can be expanded to any size so long as blood flow is not unduly impeded. Additionally, the femoral artery and vein and the jugular vein are relatively long and straight blood vessels. This will allow for the convenient insertion of a catheter having a temperature controlled region of considerable length. This is of course advantageous in that more heat may be transferred at a given temperature for a catheter of a given diameter if the length of the heat transfer region is increased. Techniques for inserting catheters into the above mentioned blood vessels are well known among medical personnel. Although the method of the present invention will probably be most commonly employed in a hospital, the procedure need not be performed in an operating room. The apparatus and procedure are so simple that the catheter may be inserted and treatment may begin in some cases even in an ambulance or in the field.

FIG. **2** depicts still another means for transferring heat to or from the distal end of a catheter. In this embodiment, catheter shaft **20** has two lumens running through it. Fluid flows from the proximal end of the catheter through in-flow lumen **60**, through a heat transfer region **62**, and back out through outflow lumen **64**. By supplying either warmed or cooled fluid through inflow lumen **60**, heat may be transferred either to or from the patient's blood stream which flows in heat transfer proximity to the heat transfer region. The heat transfer region **62** may be in the form of a balloon **70**. Use of a balloon may be advantageous in some embodiments to provide an increased surface area through which heat transfer may take place. Balloon inflation is maintained by a pressure difference in the fluid as it flows through in-flow lumen **60** and outflow lumen **64**. The balloon should be inflated to a diameter somewhat less than that of the inside diameter of the blood vessel so as not to unduly impede the flow of blood through the vessel.

FIG. **3** depicts a catheter having an internal resistance heating element **28** and a balloon **70**, which is shown inflated. The balloon surface may be provided with structures that increase the surface area available for heat transfer, i.e. fins. In this embodiment, the increased surface area provided by the inflated balloon is augmented by the presence of a set of longitudinal fins **75** on the surface of the balloon. As shown in FIGS. **3** and **4**A–C, longitudinal fins **75**, radial ribs **77**, or one or more spiral fins **79** may be disposed directly on the body **20** of a catheter. Longitudinal ribs may be advantageous because they tend to restrict blood flow through the vessel less than other configurations. In fact, these ribs insure that the balloon will not substantially block the flow of blood through the vessel because a flow path may be maintained between the ribs even when the balloon is inflated. Inclusion of a balloon on a catheter employing resistance heating allows for designs in which current is conducted through the fluid which fills the balloon.

A catheter according to the present invention may be designed and configured to optimize the rate of heat transfer between the catheter and blood flowing through the vessel. While a large surface area is desirable in order to maximize heat transfer, the catheter should be appropriately configured and sized to minimize restriction to flow through a blood vessel. Furthermore, the temperature of the catheter should be carefully controlled to prevent undesirable chemical changes within the blood. This is especially important when applying heat to the blood as blood is readily denatured by even moderately high temperatures. The exterior temperature of a catheter for warming blood should generally not

exceed about 42° C.–43° C. It is estimated that a catheter whose surface temperature is controlled between 37° C. and 42° C. will provide a body core warming rate of approximately one to two degrees Celsius per hour in a patient starting out with severe hypothermia. This estimate is highly dependent on a number of factors including the rate of blood flow through the vessel, the initial body temperature of the patient, the external surface area of the catheter through which heat is conducted, etc. The actual rate achieved may vary substantially from the above estimate. The above estimate provides a starting point for a rough estimate as to the level of power transferred from the catheter to the patient's body and therefore of the size of the power supply required by the system. Regardless of the exact means of power transmission chosen, resistance heating coil, laser and diffusing tip, direct conduction or fluid circulation, an appropriate power supply will be required to provide heat to or remove heat from the system.

The sum of heat entering and leaving a patient's body can be written as:

$$\Delta H = H_c + H_f - H_e$$

where ΔH is the sum of all heat transferred, H_c is the heat transferred from the catheter to the patient, H_f the heat produced by the patient internally, and H_e the heat lost from the patient to the environment. If one assumes, as will ordinarily be the case in a healthy patient, that the body's internal thermoregulatory system will produce just enough heat to offset heat lost to the environment, then the equation is made simple:

$$\Delta H = H_C.$$

The above equation can be written in terms of the change in the patient's internal body temperature over time as follows:

$$mc(\Delta T/\Delta t) = (\Delta H_c/\Delta t)$$

where m is the body mass of the patient, c is the specific heat of the patient's body, (ΔT/Δt) is the time rate of change of the patient's internal body temperature, ($\Delta H_c/\Delta t$) is the time rate of heat delivery from the catheter to the patient. If one assumes a patient having a body mass of 75 kilograms and a specific heat of 4186 joules/° C.-kg (assumes the specific heat of the human body to be the same as that of water, the actual value will be somewhat different), then a warming rate of 1° C. per hour (3600 seconds) will require the catheter to transfer heat to the patient at a rate of about 87 watts (1 watt=1 joule/sec). However, as an estimate of the desirable size of a power supply to be used with a catheter of the present invention, this estimation may be too low. This may be true for a number of reasons. First, it was assumed for the sake of convenience that the patient's internal system would produce an amount of heat equal to that lost to the environment. In a hypothermic patient this will obviously not be the case. Almost by definition, accidental hypothermia occurs when a person's ability to produce heat internally is overwhelmed by heat lost to the environment. The catheter will have to make up the difference so the power level required will need to be greater for that reason alone. Alternatively, to induce hypothermia, sufficient heat will need to be removed from the blood to lower the temperature of the target tissue, or in the case of whole body hypothermia, to remove more heat than is generated by the body. In removal of heat, the power required to cool the heat exchanger will be largely dependent on the efficiency of the cooling device including the dissipation of excess heat from the device to the environment.

The above estimate does not allow for power losses between the power supply and whatever warming means is utilized. Such losses could include resistance losses in electrical transmission lines between the power supply and a resistance heating element, inherent inefficiencies and other losses in a system having a laser and a diffusing tip, heat losses along a thermally conductive shaft or fluid circulation lumen, and the like. Any such losses which do occur will need to be compensated for by additional power supply capacity. Furthermore, it would be undesirable to limit the performance of a catheter according to the present invention by limiting the size of the power supply used. It would be preferable instead to use a power supply capable of providing power considerably in excess of that actually needed and then controlling the delivery of that power according to the measured temperature of the catheter itself. As mentioned previously, this can be readily accomplished by including a sensitive temperature sensor within the body of the catheter. Nevertheless, the above calculation can be used as a useful estimate of the likely lower bound for sizing a power supply for use in a catheter according to the present invention.

An alternative estimate can be made by comparing the likely performance of the various embodiments described herein with the power requirements for the external blood warming apparatus presently known. Such external warming apparatus generally requires a supply of power on the order of 1000–1500 watts and sometimes more. A device formed in accordance with the present invention may require considerably less power than that. First, the present invention may not require an external pump to circulate the blood; this function is provided by the patient's own heart. Accordingly, no power is needed to drive such a pump. Secondly, the present invention may be considerably less complicated than external blood warming systems. Known systems circulate the blood over a relatively lengthy path from the patient, through the warming element, and back into the patient. More heat may be lost over this lengthy path than in devices described herein. Thus, the power required by external blood circulation and warming systems of the type previously known can be used as a rough estimate of the likely upper limit for power required by a system according to the present invention. It is most likely that such a system may be equipped with a power supply having a capacity somewhere between the two rough estimates described above. It is therefore contemplated that a suitable power supply will be capable of providing peak power somewhere in the range between 100 and 1500 watts, probably being in the range between 300 and 1000 watts. The ranges specified are an estimate of suitable peak power capability. The power supply will most commonly be thermostatically controlled in response to a temperature sensor in the body of the catheter. The actual effective power transmitted to the patient will therefore typically be much less than the peak power capacity of the system power supply.

The above calculations refer primarily to a system for heating the blood. With respect to a catheter for cooling the blood, the temperature and power constraints may not be as limiting. Care should be taken to avoid freezing the blood or inducing shock to the patient from excessively rapid cooling. The primary component of blood is essentially water with a number of suspended and dissolved substances. As such, its freezing point is somewhat below 0° C. However, a catheter adapted to cool blood in a hyperthermic patient or to induce an artificial hypothermia will usually not be operated at temperatures that low. It is presently contemplated that the external surface of such a catheter may be

held in the range between about 1° C. and 20° C., although the actual temperature could vary between about 0° C. and the patient's current body temperature. Additionally, for example, of the case of a heat exchange balloon of some length, the surface temperature of the balloon may vary along its length as it gives off heat to the blood. A balloon may vary in temperature as much as 12° C. or more along its length.

Another aspect of the present invention further provides methods for both raising the body temperature of initially hypothermic patients and lowering the body temperature of patients who are initially hyperthermic, or for whom the body temperature is to be lowered below normal for some other purpose. In such cases, it is generally necessary to monitor the target tissue (which in whole body hypothermia may be the whole body and in regional may be, for example, the brain) and control the cooling so the desired temperature will not be exceeded for example, by the physiologic response of the patient. In such cases, this aspect of the invention specifically provides for reversing the heat transfer process to maintain the target tissue at the selected temperature.

As set forth in FIG. **5**, a sample control scheme is provided herein for either warning or cooling target tissue to a preferred temperature and maintaining the tissue at about the preferred temperature. The control scheme is described by the flow chart shown in FIG. **5** and illustrated with the graph shown in FIG. **6**. A preferred temperature is pre-selected for the target temperature, for example a temperature of 31° C. for the brain tissue. This pre-selected temperature is communicated to a control unit, for example by setting a desired temperature on a control unit for a heat exchange catheter. A heat exchange catheter capable of either removing heat from the blood or adding heat to the blood is inserted so that it is in heat exchange proximity with blood in a blood vessel that delivers blood to a target location such as the brain. The catheter is controlled by the control unit described above that may turn the heat exchanger off or on and may control the heat exchanger to heat or cool the blood which is in heat exchange proximity with the heat exchanger.

The temperature of the brain is monitored, for example by a temperature probe inserted into the brain tissue or by measuring temperature at some proxy location such as the tympanic membrane or nasal cavity provides a temperature measurement that represents the brain temperature. This results in a sensed temperature measurement that is communicated to the controller. An upper variance set point is determined, for example ½ degree above the pre-selected temperature, and communicated to the controller. In this example, that would result in an upper variance set point of 31½. A lower variance set point is also determined and communicated to the controller, for example ½ degree below the pre-selected temperature, resulting in this example in a lower variance set point of 30½°.

When the heat exchanger is cooling, the sensed temperature of the target tissue is compared with the pre-selected temperature. If the sensed temperature is above the pre-selected temperature, the cooling continues. If the sensed temperature falls to the pre-selected temperature or below, then the controller acts to turn the heat exchanger off. After the heat exchanger is turned off, the temperature of the target tissue is again measured to obtain a sensed temperature. If the sensed temperature is above the upper variance set point, the controller acts to cause the heat exchanger to begin cooling again. This cooling continues until the temperature again reaches the pre-selected temperature. At this point, the controller once again acts to turn the heat exchanger off. If the patient's body is generating heat in the target tissue at a rate greater than the loss to the environment, it may be seen that the temperature will oscillate between the preferred temperature and the upper variance set pont, in this example, between 31° C. and 31½° C. as illustrated by section A of FIG. **6**.

In some instances, the temperature of the target tissue may continue to fall spontaneously after the heat exchanger is turned off, for example if the brain tissue is giving off more heat to the environment than is generated by the brain. In such a situation the sensed temperature may continue to fall until it is below the lower variance set point. If it does, the controller acts to cause the heat exchanger to add heat to the blood and thus to the target tissue until the sensed temperature is again at the pre-selected temperature. The controller then turns the heat exchange catheter off. If the temperature again falls until it reaches a temperature below the lower variance set point, the process is repeated. If this situation repeats, it may be seen that the temperature will oscillate between the pre-selected temperature and the lower variance set point, in this example, between 31° C. and 30½° C. as illustrated by section B of FIG. **6**.

The example given here was for purposes of illustration only and many variations will be anticipated within the scope of this invention. For example, the pre-selected temperature and upper and lower variance set points may be different than those described above. The discussion above was an example of cooling the target tissue to a temperature below normothermic. However it may be seen that a pre-selected temperature above normothermic may also be selected, and a heat exchanger which is controlled to both add heat to the blood or remove heat from the blood may, through use of the same control scheme, maintain the temperature of the target tissue at the preferred temperature within the upper and lower variance set points around a pre-selected temperature above normothermic. It may also be readily perceived that a patient that is hypothermic may be rewarmed to normothermia by setting the preselected temperature in the control scheme illustrated to 37° which will cause the heating element to warm the blood until the sensed temperature reaches 37°. The anticipation and prevention of temperature overshoot may be accomplished as described in U.S. patent application Ser. No. 08/584,013 previously incorporated herein by reference.

In the example given, the steps are all stated as discrete actions, such as measuring the temperature of the target tissue or comparing sensed and pre-selected temperatures, but it may be readily understood by one of skill in the art that the actions may be relatively continuous. It will also be readily appreciated that control criteria other than the temperature of the target tissue may be substituted and controlled, for example blood pressure or cranial pressure, or temperature derived from some other location, and two control schemes as described may be simultaneously instituted for different locations in the patient, for example, to cool a region such as the brain and maintain that region in a relatively stable cooled condition while simultaneously warming the core temperature of the patient to normothermic and maintaining the patient's core temperature relatively stable at a normothermic temperature. The method of affecting the target tissue's temperature discussed above was cooling the blood upstream from the target tissue, but it may be appreciated that other methods of heating and cooling, for example heating or cooling cerebrospinal fluid circulating around the brain or spinal cord may be employed.

A system for the selective warming and cooling of patients is illustrated in FIG. **7**. The system may comprise a

catheter **100** having a proximal end **102**, a distal end **104**, a heat-generating surface **106** near the distal end, and a heat-absorbing surface near the distal end **108**. The heat-generating surface **106** may include any of the heat transfer components described above, particularly a wire coil resistance heater as shown having from 50 to 1000 windings, typically spaced-apart from 0.1 mm to 1 mm. The total length of the catheter may range from 15 cm to 50 cm, and may measure from about 1 mm to 5 mm in diameter. The windings may extend over a total distance in the range from 10 cm to 20 cm near the distal end. The heat-absorbing surface may be a thermally conductive metal foil, typically composed of a biologically compatible thermally conductive metal, such as gold, silver, aluminum, or the like. Copper may also be useful, but should be treated or encapsulated in order to enhance its biocompatibility. The metal foil may be thin in order to enhance flexibility of the catheter body, typically having a thickness in the range from 0.001 mm to 0.01 mm. The heat-absorbing surface **108** may be conductively coupled to a cooler located externally of the catheter, typically in a control unit **120** as described below. In the illustrated embodiment, the surface **108** is coupled by a thermally conductive core member **110** composed of a flexible rod or wire formed from one of the thermally conductive metals described above. Alternatively, thermal coupling can be achieved by extending the surface **108** proximally so that the proximal end of the surface can be coupled to the cooler. In the latter case, it may be preferable that the proximal portions of the surface **108** be thermally insulated to prevent cooling outside of the blood circulation. The system may further comprise a control unit **120** which typically provides both the heat-generator and the cooler for coupling to the catheter **100**. The heat-generator may also comprise a direct current source for coupling to the resistance heater on the catheter. Usually, the direct current source will be a commercially available, temperature-controlled DC power supply, typically operating at a voltage in the range from 10 VDC to 60 VDC and a current output in the range from 1 A to 2.5 A. The power supply may be controlled to maintain the surface temperature of the heating surface **106** in the range from 40° C. to 42° C. As discussed above, the surface temperature should not exceed 42° C. in order to prevent damage to blood components. Other desirable characteristics of the heat exchange surface are described above.

Alternatively, the temperature of the heat exchange surface can also be controlled based on measured blood temperature and/or measured body temperature. Blood temperature can be measured by temperature sensors present on the catheter. For example, a temperature sensor **112** may be located on the catheter spaced-apart from the heat exchange surfaces **106** and **108**. The temperature sensor **112** may be located either upstream or downstream from the heat exchange surfaces based on the direction of blood flow and depending on the manner in which the catheter is introduced to the patient. Optionally, a pair of temperature sensors could be provided, one disposed on each side of the heat exchange surfaces in order to measure both upstream and downstream blood temperatures. The catheter may also include a temperature sensor (not shown) coupled directly to the heat-generating surface **106** so that the temperature of the surface may be directly controlled. Other temperature sensors (not shown) may be provided for directly measuring the patient's core body temperature or the temperature of various regions of the patient's body, with the temperatures being fed back into the control unit **120**. The cooler in control unit **120** may be any type of refrigeration unit capable of removing heat from the heat-absorbing surface **106** at a rate sufficient to cool the blood at a desired rate. Typically, the cooler may be rated at from 150 W to 350 W.

The cooler will be a thermoelectric cooler, such as those commercially available from Melcor Thermoelectrics, Trenton, N.J. 08648. The cooler may be directly coupled to the core element **110** so that direct heat conduction from the heat-absorbing surface **108** may be effected to the cooler in control unit **120**. The temperature of the cooling surface **108** may be less critical than that of the heating surface **106** with regard to this aspect of the invention, but will usually be maintained in the range from 0° C. to 35° C. preferably being below 30° C. The temperature of the cooling surface may be directly controlled within this range, or alternatively, the system may be designed so that the cooling temperature operates approximately within this range based on the total system characteristics.

The control unit **120** may further include one or more temperature controllers for controlling the temperature of the heat-generating surface **106** and the heat-absorbing surface **106** based on the blood temperature and/or the body temperature. At a minimum, the control unit **120** may control the temperature of the heat-generating surface **106** within the range set forth above, and may monitor at least one of the patient blood temperature and patient body temperature in order to reverse the heating or cooling mode as discussed above. With respect to the control scheme described in FIG. **10**, for example, the system may operate in an on-off mode where for example hypothermic patients are initially treated by warming the blood at a constant surface temperature rate until a target temperature is reached. When the target temperature is reached, power to the heat-generating surface **106** is turned off. Monitoring of the blood and/or patient body temperature, however, is maintained to assure that the patient temperature does not exceed a maximum which is above the target temperature. Should the maximum be exceeded, then the system is operated in the cooling mode until the excess body temperature is lowered. Usually, there will be no need to again warm the patient, but the present system may provide for further cycles of warming and cooling if necessary. For initially hyperthermic patients, the cooling and warming modes are reversed. It will be. appreciated that the temperature control schemes of the present invention could be substantially more sophisticated. For example, the power input, to warm the patient could be controlled based on proportional, derivative, or integral control schemes which will typically provide for a tapering of the heat transfer rate as the patient's core or regional body temperature approaches the desired target level. Moreover, cascade control schemes based on both patient blood temperature and patient body temperature could be devised. Such control schemes, for example, could be adapted both for warming the patient and cooling the patient with mathematical models of typical patient physiological characteristics being taken into account in preparing the control schemes. However, a simple off-on control scheme that is capable of reversing the heat transfer mode if the target temperature is exceeded by more than a safe amount will be sufficient.

Another aspect of the invention provides methods and apparatus for regulating the temperature of a fluid that is to be delivered to a target location within a patient while the fluid is within the body. The regulation of the fluid temperature in this manner lends itself to a variety of applications including heating or cooling the temperature of drugs, solutes, or blood before their delivery to a target site. Regulation of the temperature of the injected fluid may also

find use in regulating the temperature of the target location itself in preparation for various medical procedures, including neurosurgical procedures within the brain. Further, the methods and apparatus allow for the temperature of tissue within a patient's body temperature to be controlled by warming or cooling the patient's blood in situ. By warming or cooling the patient's blood that subsequently flows to that tissue, the temperature of the tissue in question may thereby be increased or decreased as desired. Such methods and apparatus therefore provide a convenient therapy for treating hypothermia or hyperthermia, or for inducing regional cooling or heating.

FIG. **8** depicts a distal end **210** of a catheter **212** formed in accordance with another aspect of the present invention. The catheter **212** may be positioned within a blood vessel BV. Blood flow through the vessel is indicated in FIG. **8** by a set of arrows F. The distal end **210** of the catheter **212** may include a temperature altering region **214** although it will be appreciated that the temperature altering region may be located anywhere between the proximal and the distal catheter end. Techniques for inserting catheters into various blood vessels such as the Seldinger technique mentioned above, are well known among medical personnel. The catheter **212** may be manufactured in various sizes depending upon the particular application. For most uses, it may have a length in the range from about 30 cm to about 130 cm, and a diameter in the range from 6 to 12 French (1 French=0.33 mm). The catheter **212** will preferably be flexible to allow the catheter to be moved through various vessels within a patient, and may be positioned in the body preferably with the assistance of a guidewire.

As shown in FIG. **9**, the catheter **212** may include an internal lumen **216**. A temperature altering mechanism **218** may be provided adjacent the luminal wall of the lumen **216** at the temperature altering region **214**. For convenience of discussion, the temperature altering mechanism **218** is illustrated schematically and may comprise a variety of mechanisms that are employed to either heat or cool the luminal wall of the lumen **216** to heat or cool the fluid passing through the lumen **216** at the temperature altering region **214**. Exemplary mechanisms for heating or cooling the luminal wall may include heated or cooled fluids passing through the catheter **212** near the luminal wall, resistive elements disposed within the catheter **212**, laser energy that is supplied to the temperature altering region, various chemicals disposed within the catheter body, thermoelectric crystal, and the like. Use of such mechanisms allow fluids passing through the lumen **216** at the temperature altering region **214** to have their temperature altered so that they will be within a desired range when exiting the catheter **212**. The temperature altering mechanism **218** may be configured to heat a fluid passing through the temperature altering region so that its temperature will be heated by at least 5° C. to about 42° C. When cooling a fluid, the temperature altering mechanism **218** may be configured to cool the fluid by at least 7° C. to about 30° C. The temperature altering mechanism **218** may be designed to optimize the rate of heat transfer between the catheter and a fluid flowing through the internal lumen. Further, the temperature of the catheter may be carefully controlled to prevent undesirable chemical changes within the blood. This is especially important when applying heat to the blood as blood is readily denatured by even moderately high temperatures. The temperature of the luminal wall for warming blood should generally not exceed about 42° C. to 43° C. The amount of energy that may be supplied to heat a patient's core body temperature is described in U.S. Pat. No. 5,486,208, previously incorporated by reference herein. The temperature altering mechanism **218** may be also arranged within the catheter **212** so that the temperature of the luminal wall may be heated or cooled without substantial direct heating of an outer surface of the catheter. In this way, the catheter **212** may be employed to selectively heat or cool a specific target site by simply positioning the distal end of the catheter at the target site and introducing a fluid through the lumen **216**.

As shown in FIGS. **9** and **10**, a catheter **220** formed in accordance with this aspect of the invention may circulate a heat transfer fluid to alter the temperature of a fluid passing through the catheter. The catheter **220** comprises a catheter body **222** having a proximal end **224** and a distal end **226**. A lumen **228** extends between the proximal end **224** and the distal end **226**. At the proximal end **224**, is a proximal port **230** through which various fluids may be introduced into the lumen **228** from outside of a patient. Passing through the catheter body **222** is a first fluid path **232** and a second fluid path **234** as particularly shown in FIG. **10**. A first port **236** is in communication with the first fluid path **232** and a second port **238** is in communication with the second fluid path **234**. In this manner, a heated or cooled heat transfer fluid may be introduced into the first port **236** where it passes through the first fluid path **232** adjacent to the lumen **228**. As the heat transfer fluid passes through the first fluid path **232**, heat is transferred either to or from a fluid passing through the lumen **228** to heat or cool the fluid to a desired temperature before exiting the catheter body **222**. After passing through the first fluid path **232**, the heat transfer fluid circulates back through catheter body **222** through the second fluid path **234** where it exits the second port **238**.

FIGS. **11** and **11A** provide illustrations of yet another variation of the invention that includes a catheter **240** with resistive heating to heat a fluid passing through the catheter. The catheter **240** comprises a catheter body **242** having a proximal end **244** and a distal end **246**. A lumen **248** passes through the catheter body **242** between its proximal end **244** and distal end **246**. A proximal port **250** is provided to facilitate the introduction of fluids into the lumen **248** from outside a patient. Disposed within the catheter body **242** near the lumen **248** are a plurality of wires **252** as shown in FIG. **17**. These wires **252** may exit the catheter body **242** through a port **254**. The wires **252** may be also connected to either a DC or low frequency AC power supply. As electrical current passes through the wires **252**, some of the energy is dissipated as heat to heat the luminal wall. Alternatively, a radio frequency or RF power supply may be employed to supply power to electrodes disposed within the catheter body **242** to heat the luminal wall.

Referring now to FIGS. **12–14**, a catheter **256** may be employed to heat or cool an externally injected fluid, to heat or cool a body fluid in situ, or a combination of both. The catheter **256** may comprise a catheter body **258** having a proximal end **260** and a distal end **262**. Extending between the proximal end **260** and the distal end **262** is a lumen **264** as shown in FIG. **12**. A proximal port **266** is also provided at the proximal end **260** to allow various fluids to be injected into the lumen **264** while port **266** is positioned outside a patient. At the distal end **262** is a temperature altering region **268** which includes a temperature altering mechanism (not shown). The particular temperature altering mechanism may comprise any of those described with respect to other aspects of the invention set forth above or hereafter. In this manner, a fluid which is injected into the port **266** will pass through the lumen **264** and have its temperature altered when passing through the temperature altering region **268** in a manner similar to that previously described with other

embodiments. The catheter body **258** may include a plurality of perfusion orifices **270** which extend through the wall of the catheter body to provide fluid paths to the lumen **264**. As shown by the arrows in FIG. **12**, a body fluid, such as blood, may pass through the orifices **270** and into the lumen **264** where it will have its temperature altered at the temperature altering region **268** so that the temperature of the body fluid will be within a desired range when exiting the catheter body **258** at its distal end **262** as shown.

As illustrated in FIGS. **13** and **14**, the luminal wall of the catheter body **258** may include a plurality of flaps **272**. These flaps **272** may control the passage of body fluids through the orifices **270** and into the lumen **264**. These flaps **272** or similar structures may be also constructed as described in U.S. Pat. No. 5,180,364, the disclosure of which is herein incorporated by reference. When a fluid is injected into the lumen **264** at the port **266**, the pressure and direction of flow of the injected fluid will cause the flaps **272** to close over the orifices **270** as shown in FIG. **13** so that essentially only the injected fluid will pass through the temperature altering region **268**. In this way, the temperature of the injected fluid will have its temperature altered so that it will be within a desired range when exiting the distal end. As shown in FIG. **14**, when no fluids are injected into the port **266**, the pressure of the body fluid within a vessel will cause the flaps **272** to open to allow the body fluids to flow through the orifices **270** and into the lumen **264**. In this manner, a body fluid, such as blood, may have its temperature altered by passing through the orifices **270** and through the temperature altering region **268**. The configuration of the flaps **272** is particularly advantageous in applications where the temperature of a patient's tissue is altered. By simply introducing the catheter **256** into the patient, the blood which flows into the lumen **264** via the orifices **270** will have its temperature altered by the time it exits the distal end **262**. This may result in whole body temperature alteration, or if the blood is directed to a specific site by the catheter, may result in regional temperature alteration. In the event that a solute or drug is also needed for therapy, it may be introduced into the lumen **264** through the port **266** and have its temperature be substantially the same as the exiting blood temperature. As described above, this aspect of the invention provides methods and apparatus which are useful in regulating the temperature of various fluids while such fluids are within a patient. With such an arrangement, a variety of procedures may be performed including the introduction of a drug or solute from outside the patient that may have its temperature altered within the catheter before reaching a target location. Furthermore, a fluid may be heated or cooled within the catheter to in turn heat or cool a specific region of a body structure prior to the performance of a medical procedure. In another alternative, the temperature of a patient's body fluid, such as blood, may be altered in situ to treat a patient suffering from either hypothermia or hyperthermia, or to intentionally induce either whole body or regional hypothermia.

Another aspect of the present invention provides methods and apparatus for regional and whole body temperature modification. The lowering of body temperature for selected regions may provide a neuroprotective effect particularly in proximity to the brain. Selected portions of at least one catheter may, for example, cool fluids such as blood or cerebral spinal fluid that are in contact with, circulating in, around, or leading to the brain region. The cooled body fluid may be selectively directed to a chosen region of the patient's body for producing a regionally confined cooling effect. Alternatively, a patient's whole body temperature may be reduced to provide, for example, neuroprotection for the entire brain and other widely spaced tissue such as the spinal cord. As will be discussed in further detail below, methods and apparatus provided herein may include a heat exchange catheter formed with an increased surface area or a finned section to provide rapid and effective heat transfer. A regionally confined thermal transfer region along a catheter body having a longitudinal dimension may further provide effective heat transfer with fluids traveling within an inner passageway, while the catheter may further provide a zone of regional cooling or heat transfer along selected portions of the catheter. Various combinations of both heating and cooling elements may be defined along different portions of a single catheter, or as part of a series or combination of heat exchange devices as similarly described with respect to other aspects of the invention. All of these devices and procedures may be directed to regional or selected body temperature modification that is particularly suitable for the cooling of the cerebral region, and for inducing an artificial state of hypothermia that may provide therapeutic benefits in the treatment of cerebrovascular injury. The system may be a simple heat transfer catheter with manual controls, or may be operated by means of a controller that may monitor a number of sensors and control the heat exchange catheter in response to data received form said sensors.

As generally shown in FIG. **15**, a heat transfer catheter system directed to this aspect of the invention may include a catheter control unit **300** and a heat transfer catheter **302** formed with a combination of at least one heat transfer section. The heat transfer section or sections are located on that portion of the catheter, as illustrated by section **319**, that is inserted into the patient. This insertion portion is less than the full length of the catheter and extends from the location on the catheter just inside the patient, when the catheter is fully inserted, to the distal end of the catheter. The catheter control unit **300** may include a fluid pump for circulating a heat exchange fluid or medium within the catheter **302**, and a combination of at least one heat exchanger component for heating and/or cooling circulating fluids within the heat transfer system. A reservoir or fluid bag **306** may be connected to the control unit **300** to provide a source of heat transfer fluid such as, saline, blood substitute solution or other biocompatible fluid. The control unit **300** may further receive data from a variety of sensors which may be, for example, solid state thermocouples to provide feedback and patient temperature information from selected organs or portions of the body such as a temperature probes for the brain and head region **308**, a rectal temperature probe **309**, an ear temperature probe **311**, a bladder temperature probe (not shown) and the like. Based upon sensed temperatures and conditions, the control unit **300** may direct the heating or cooling of the catheter in response to input from the sensors. The control unit **300** may activate a heat exchanger at a first sensed temperature, and may also deactivate the heat exchanger at a second sensed temperature which may be relatively higher or lower than the first sensed temperature or any other predetermined temperature. The control unit **300** may of course independently heat or cool selected heat transfer sections to attain desired or preselected temperatures in body regions. Likewise the controller may activate more than one heat exchanger to control temperature at particular regions of the patient's body. The controller might also activate or deactivate other apparatus, for example, external heating blankets or the like, in response to sensed temperatures. The controller may function as described above and illustrated in FIGS. **5** and **6**.

The temperature regulating catheter **302** illustrated in FIG. **15** may also provide various zones of cooling and/or heating by circulating heat transfer medium through a series of inlet and an outlet conduits. A first and a second fluid path **312** and **314** may provide a heat exchanger channel within the catheter, and may be respectively connected to the inlet **316** and outlet **317** of a pump for circulation of a heat transfer fluid to cool the flow of fluid within a selected body region. A similar arrangement may be implemented for heating a selected body region simultaneously or independently from the cooling component of the system. The catheter control unit **300** may further include a thermoelectric cooler and heater which are selectively activated and deactivated to perform both heating and cooling functions with the same or different heat transfer medium within the closed-loop catheter system. For example, a first heat transfer section **318** of at least one temperature regulating catheter **302** and located on the insertion portion **319** of that catheter, may circulate a cold solution in the immediate head region, or alternatively, within a carotid artery or other blood vessel leading to the brain. The head temperature may be locally monitored with temperature sensors **308** positioned on a relatively proximate exterior surface of the patient or within selected body regions. Another or a second heat transfer section **320** of the catheter **302**, also located on the insertion portion **319**, may circulate a heated solution within a collapsible balloon or otherwise provide heat to other body locations through heating elements other mechanisms described in accordance with other aspects of the invention. While the heat transfer catheter **302** may provide regional hypothermia to the brain region for neuroprotective benefits, other parts of the body may be kept relatively warm so that adverse side effects such as shivering may be avoided or minimized. Warming of the body generally below the neck may be further achieved by insulating or wrapping the relatively lower body in a heating pad or blanket **322** while the head region **310** above the neck is cooled. It should be understood of course that multiple heat transfer sections of the catheter **302** may be modified to provide whole body cooling or warming to affect body core temperature, and is not just limited to regional or localized body temperature regulation.

FIG. **16** provides an illustration of the heat transfer catheter system of the invention which includes disposable components including a heat transfer catheter **324**, a disposable heat exchange plate **338**, a pump head assembly **340**, a saline bag **339**, sensors **348**, **344** and a fluid flow line **337**, as well as reusable components including a solid state thermoelectric heater/cooler **342**, a pump driver **343** and various controls for the unit.

The heat transfer catheter **324** is formed with a blood channeling sleeve **325**, a catheter shaft **326**, and a heat exchanger **327** which may be for example a heat exchange balloon operated using closed-loop flow of heat exchange medium. The catheter shaft may be formed with a working lumen **328** for injection of drugs, fluoroscopic dye, or the like, and for receipt of a guide wire **329** for use in placing the heat transfer catheter at an appropriate location in the patient's body. The proximal end of the shaft may be connected to a multi-arm adapter **330** for providing separate access to various channels in the catheter shaft. For example, one arm **336** may provide access to the central lumen **328** of the catheter shaft for insertion of a guide wire **329** to steer the heat transfer catheter to the desired location. Where the heat exchanger **327** is a heat exchange balloon for closed-loop flow of a heat exchange medium **331**, the adapter may contain an arm **332** to connect an inlet flow line **333** to an inlet flow channel (not shown in this Fig.) within the catheter shaft, a separate arm **334** to connect an outlet fluid line **335** to an outlet flow channel (also not shown in this Fig.) A dual channel flow line **337** may contain both inlet and outlet flow lines **333**, **335** to connect the catheter shaft **326** to a disposable heat exchange plate **338**. Additionally, one of the flow lines, for example the inlet flow line **333** may be connected to a bag **339** of heat exchange fluid **331** to prime the closed-loop heat exchange balloon catheter system as necessary.

The heat exchange plate **338** may include a serpentine pathway **339** for the heat exchange fluid to be pumped through the heat exchange plate by means of a disposable pump head **340**. The heat exchange plate including the serpentine pathway and the pump head is configured to install into a reusable master control unit **341**. The master control unit may include a heat generating or removing unit **342** such as a thermoelectric heater/cooler (TE cooler). A TE cooler is particularly advantageous because the same unit is capable of either generating heat or removing heat by changing the polarity of current activating the unit. Therefore it may be conveniently controlled to supply or remove heat from the system without the need of two separate units.

The master control unit includes a pump drive **343** that activates the pump head **340** to pump the heat exchange fluid **331** and cause it to circulate through the heat exchanger **327** and the serpentine path in the heat exchange plate. When installed, the heat exchange plate is in thermal communication with the TE cooler, and thus the TE cooler may act to heat or cool the heat exchange fluid as that fluid is circulated through the serpentine pathway. When the heat exchange fluid is circulated through the heat exchanger located in a patient's body, it may act to add or remove heat from the body. In this way the TE cooler may act to affect the blood temperature of a patient as desired.

The TE cooler and the pump are responsive to a controller unit **344**. The control unit receives data input through electrical connections **345**,**346**, **347** to numerous sensors, for example body temperature sensors **348**, **349** that may sense temperatures from a patient's ear, brain region, bladder, rectum, esophagus or other appropriate location as desired by the operator who places the sensors. Likewise, a sensor **350** may monitor the temperature of the heat exchange balloon, and other sensors (not shown) may be provided as desired to monitor the blood temperature at the distal tip of the catheter, at the proximal tip of the catheter, or other desired location.

An operator by means of the manual input unit **351** may provide the operating parameters of the control system, for example a pre-selected temperature for the brain. The parameters are communicated to the control unit **344** by means of a connection **353** between the manual input unit and the control unit.

In practice, the operator using the manual input unit supplies a set of parameters to the control unit **344**. For example, a desired temperature for the brain region and/or the whole body of the patient may be specified as the preselected temperature. Data is received from the sensors **348**, **349** indicating for example, a sensed temperature of the patient at the location of the sensors, e.g. the actual core body temperature of the patient or the actual temperature of the brain region. Other data input may include the actual temperature of the heat exchanger, the temperature of blood at the distal end of the catheter body, or the like.

The control unit coordinates the data and selectively actuates the various units of the system to achieve and maintain parameters. For example, it may actuate the TE

cooler to increase the amount of heat it is removing if the actual temperature is above the specified temperature, or decreasing the amount of heat being removed if the temperature is below the specified temperature. It may stop the pumping of the heat exchange fluid when the body or regional temperature sensed is the desired temperature.

The controller may have a buffer range for operation wherein a target temperature is established, and an upper variance set point temperature and lower variance set point temperature are also set. In this way, the controller may cause the heat exchanger to operate until the target temperature is reached. At that temperature, the controller may suspend the operation of the heat exchanger until either the upper variance set point temperature is sensed or the lower variance set point temperature is reached. When the upper variance set point temperature is sensed, the controller would then activate the heat exchanger to remove heat from the blood stream. On the other hand, if the lower variance set point temperature is sensed, then the controller would activate the heat exchanger to add heat to the blood stream. This control scheme is similar to that illustrated in FIGS. **5** and **6** discussed above. Such a control scheme as applied to this system has the advantage of allowing the operator to essentially dial in a desired temperature and the system will act to reach that target temperature and maintain the patient at that target temperature. At the same time, a buffer range is established so that when the target temperature is reached, the controller will generally not turn the TE cooler on and off or activate and deactivate the pump drive in rapid succession, actions that would be potentially damaging to the electric units in question.

It may also be perceived, in keeping with the present invention, that the controller may be configured to simultaneously respond to several sensors, or to activate or deactivate various components such as several heat exchangers. In this way, for example, a controller might heat blood that is subsequently circulated to the core body in response to a sensed core body temperature that is below the target temperature, and simultaneously activate a second heat exchanger to cool blood that is directed to the brain region in response to a sensed brain temperature that is above the target temperature. It may be that the sensed body temperature is at the target temperature and thus the heat exchanger that is in contact with blood circulating to the core body may be turned off by the controller, while at the same time the controller continues to activate the heat exchanger to cool blood that is directed to the brain region. Any of the many control schemes that may be anticipated by an operator and programmed into the control unit are contemplated by this invention.

An advantage of the system as illustrated is that all the portions of the system that are in contact with the patient are disposable, but substantial and relatively expensive portions of the system are reusable. Thus the catheter, the flow path for sterile heat exchange fluid, the sterile heat exchange fluid itself, and the pump head are all disposable. Even if a rupture in the heat exchange balloon permits the heat exchange fluid channels and thus the pump head to come in contact with a patient's blood, no cross-contamination will occur between patients because all those elements are disposable. The pump drive, the electronic control mechanisms, the TE cooler, and the manual input unit, however, are all reusable for economy and convenience. Likewise, the sensors may be disposable, but the control unit to which they attach is reusable.

It will readily be appreciated by those of skill in the art that the system described here in detail may be employed using numerous substitutions, deletions and alternatives without deviating from the spirit of the invention as herein claimed. For example, but not by way of limitation, the serpentine pathway may be a coil or other suitable configuration, the sensors may sense a wide variety of body locations and other parameters may be provided to the control unit, such as temperature or pressure, the heat exchanger may be any appropriate type, such as a thermal electric heating unit which would not require the circulation of heat exchange fluid. If a heat exchange balloon is provided, a pump might be provided that is a screw pump, a gear pump diaphragm pump, a peristaltic roller pump, or any other suitable means for pumping the heat exchange fluid. All of these and other substitutions obvious to those of skill in the art are contemplated by this invention.

FIGS. **17**A–E provide illustrations an embodiment of a heat exchanger of the invention. As shown in FIG. **17**A, a heat exchange balloon catheter **360** with a finned balloon portion **362** may be positioned within at least a portion of the descending aorta **364** and a blood vessel **366** conducting blood flow to the brain region. It should be understood that the balloon portion **362** may be formed of material that is sufficiently thin to promote effective thermal transfer between heat exchange fluid within the balloon and blood flowing within heat exchange proximity of the balloon, but not excessively elastic to expand and unintentionally obstruct a fluid passageway or blood vessel **366**. Indeed, the use of thin, strong but relatively inelastic material such as PET is desirable to obtain a predictable balloon configuration with adequate heat exchange properties. The catheter shaft **368** of the thermal catheter **360** provided herein may be placed in a desired location relative to a selected body region or artery **366** by conventional techniques such as guiding catheters or steerable wire over-the-wire technique as known to those of ordinary skill in the field. The balloon portion **362** of the catheter **360** may support the closed-loop circulation of a heat transfer fluid as described herein. The increased surface area may provide effective heat transfer within a body region by thermal conduction, and may further permit blood continued blood flow without substantial disruption by creating channels exterior of the balloon surface when the balloon is expanded.

FIG. **17**B illustrates a heat exchange balloon **360** mounted on a shaft **368** defined by a longitudinal axis and a plurality of heat transfer fins **369**, **371**, **373**, **375** projecting radially outward from the longitudinal axis **370** of the catheter shaft. The heat transfer fins may be formed, for example, as the lobes of a multi-lobed, collapsible balloon. The shaft **368** is generally round and in this embodiment includes a working lumen **370** running through the shaft and open at the distal end of the catheter. The working lumen may be used for the injection of medicaments which may include, for example, a thrombolytic agent, an anticoagulant, a neuro-protectant, a barbiturate, a anti-seizure agent, an oxygenated perfusate, a vaso-dilator, an agent which prevents vaso-spasm, an agent to prevent platelet activation, and an agent to deter the adhesion of platelets. Alternatively, the working lumen may be used for the injection of flouroscopic dye, for the receipt of a guide wire **329**, or as a guiding catheter for various diagnostic or therapeutic devices including, for example, an angioplasty catheter, an embolectomy catheter, an occlusion member delivering catheter, an embolization member delivering catheter, an electro-cautery device, or a microcatheter. The shaft exterior of the central lumen is divided by a web **372** into two channels, an inlet channel **374** and an outlet channel **376**. The shaft has inlet orifices **377**, **378**, **379** communicating between the inlet channel and the interior of

the balloon at the distal portion of the balloon. The shaft also has outlet orifices **380, 381, 382** communicating between the interior of the balloon and the outlet channel. A plug **384** is inserted in the outlet channel between the inlet and the outlet orifices. The web **372** may be removed from the shaft between the plug and the inlet orifices to reduce resistance to flow of the heat exchange fluid in this portion of the shaft. Alternatively, in an embodiment not illustrated here, a tube with an open round lumen may be spliced between the plug in the outlet channel and the inlet orifices to provide a channel under the balloon for relatively unobstructed flow of the heat exchange fluid.

The balloon may be made of, for example, a single sheet of collapsible thin plastic material **285** sufficiently thin to allow for effective thermal exchange between a heat exchange fluid on the interior of the balloon and blood flowing over the exterior of the balloon. Tacking the material to the shaft as shown at **286** may form lobes of the balloon. Tacking the sheet of plastic to itself in appropriate locations as shown at **287** and **288** may further shape the lobes. The lobed shape of the balloon surface provides for significant surface for heat exchange while providing for continued flow past the balloon through the space between the lobes of the balloon.

In use, heat exchange fluid (not shown) may be pumped under mild pressure into the inlet channel **374**. The heat exchange fluid may be, for example, sterile saline or other biocompatible fluid with appropriate heat transfer characteristics. The heat exchange fluid flows down the inlet channel until it reaches the inlet orifices **377, 378, 379** at the distal end of the balloon. The fluid flows from the inlet channel into the interior of the balloon. It then flows in a proximal direction through the interior of the balloon until it reaches the outlet orifices **380, 381, 382** at the proximal end of the balloon. The heat exchange fluid then flows from the interior of the balloon through the outlet orifices and into the outlet channel **376** where it then flows back down the shaft and out of the body.

In the manner described above, a heat exchange fluid may be circulated through the balloon and either give off heat if the fluid is hotter than the blood flowing past the balloon, or absorb heat from the heat exchange fluid is cooler than the blood.

FIGS. **18A–E** provide illustrations of another variation of the invention heat exchange catheter **390** formed with a sleeve having an inner fluid passageway **392** that provides regionally confined thermal transfer. The heat transfer catheter **390** may comprise a blood channeling sleeve **394** for placement within a fluid-containing body region, the sleeve defined by a proximal region **396** and a distal region **398** formed with an inner fluid passageway **392** defined by at least one relatively proximal opening **395** and at least one relatively distal opening **399** each in communication with the fluid-containing body region for directing the flow of fluid within the catheter body **394**. A heat exchanger is internally positioned within at least a portion the sleeve for regionally confined heat transfer with fluid within the inner fluid passageway **392** of the blood channeling sleeve. In FIGS. **18A–E** the heat exchanger illustrated is a fluted closed-loop exchanger positioned around the circumference of the interior passageway **392** for circulation of heat exchange fluid as described in greater detail below.

As shown in FIG. **18A**, the temperature regulating catheter **390** may be positioned within at least a portion of the aorta **364** and a blood vessel **399** branching off the aorta to direct blood to the brain region. The catheter is positioned in the innominate artery, but could equally be positioned, for example, with its distal portion in the right common carotid artery, the left common carotid, the right internal carotid and the left internal carotid among other locations. Blood may therefore be directed into the brain region while passing the heat exchanger positioned within the inner fluid passageway **392** of the catheter body **394**. When the heat exchanger is configured for cooling blood flowing through the inner passageway **392** and the catheter is positioned as shown in FIG. **24A**, localized hypothermia of the brain region may be effectively achieved. The temperature regulating catheter **390** may be also selected for applicable methods for controlling the temperature of other selected fluid-containing body regions, for example, where the catheter is positioned to selectively direct blood to those regions.

As illustrated in greater detail in FIGS. **18B–G**, the catheter may be formed with a proximal shaft **400**, the proximal shaft having a central working lumen and two arc-shaped lumens in side-by side configuration. The two lumens comprise an inlet lumen **402** and an outlet lumen **403**. The blood channeling sleeve is attached to the proximal shaft at a proximal attachment region **404**. The sleeve comprises a layer **405** of very thin material such as a PET sheet formed into a large tube-like configuration. The catheter shaft is positioned down the inside of the tube, and the sheet is attached along both the top **406** and the bottom **407** of the catheter shaft along the length of the sleeve. This creates two wing -like channels **408, 409** on each side of the catheter running the length of the sleeve that are the inlet and outlet channels respectively. The outer layer of the plastic sheet of each of these channels may be connected together at the top of the channels **410** to form the tube-like structure that forms the sleeve. In addition, the two layers of plastic sheet that form each channel may be connected together at various points or along lines **411** along the length of the sleeve to form pleats **412**, and the inner layer **405** may be loose so that the channels will billow when inflated.

At the proximal end of the sleeve, just distal of the attachment region **404**, an orifice **415** is formed between the inlet lumen **402** and the inlet channel of the catheter shaft **409**, and similarly an orifice **416** is formed between the outlet lumen **403** and the outlet channel **408** of the sleeve. At the distal portion of the sleeve, the inlet **409** and outlet **408** channels between the plastic sheets are connected, so that there is a common space **413** shared by the two channels to allow fluid flowing down the inlet side to be removed through the outlet side as described in greater detail below. The catheter shaft under the sleeve may have reduced profile as illustrated in FIG. **18B** so that the sleeve formed of the thin plastic sheets may be folded down onto the catheter shaft and have a suitably low profile.

As an alternative method of construction, two tubes may be used to create the sleeve. The catheter shaft is inserted into a large outer tube, and a slightly smaller inner tube is inserted into the outer tube but over the catheter shaft. The outer tube is sealed along its length on the bottom of the catheter shaft, and the inner tube is sealed along its length on the top of the catheter shaft. The inner and outer tubes are sealed to each a line opposite the catheter shaft to form two channels between them. The seal opposite the shaft does not extend all the way to the distal end which functions to create the common space for communication between the inlet and outlet channels.

Yet another method of constructing such a device is to invert a large tube of thin plastic to create an inner passageway bounded by two layers of thin plastic, with the thin plastic layers essentially attached at their distal end. The space between the two plastic layers forms the inlet and

outlet channels. The catheter shaft may be placed within the inner passageway, and the two layers sealed to each other and to the catheter shaft along the bottom of the catheter shaft for the length of the inner passageway. The two layers of plastic are also sealed to each other along the top of the inner passageway from the proximal opening to a point just short of the distal end of the passageway. This creates an inlet channel **409** and an outlet channel **408** while leaving a common space **413** at the distal end of the sleeve.

In use, heat exchange fluid (not illustrated) is introduced under pressure into the inlet lumen **402** of the proximal shaft **404**. It is directed down the shaft to the inlet orifice **415**, at which point it enters the inlet channel **409** between the two layers of the plastic sheet on the inlet side. The fluid is then directed down the inlet channel, essentially inflating the billowing pleats of the sleeve somewhat. The fluid enters the common space **413** at the distal end of the blood channeling sleeve, and thereby enters the outlet channel **408** formed between the layers of plastic sheet on the outlet side of the sleeve. The fluid travels back down the length of the sleeve through the pleated channel to the outlet orifice **416** formed between the outlet channel **408** and the outlet lumen **403** in the catheter shaft. The fluid then travels down the outlet channel and out of the body. In this way, heat exchange fluid may be circulated through the structure to create heat exchange between blood flowing through the inner passageway in heat exchange proximity with the heat exchange fluid.

The formation of the inner passageway using a thin plastic sheets allows blood channeling sleeve to be collapsed to a low profile, for example, wrapping or folding it onto the reduced profile portion of the catheter shaft. This in turn provides a low profile device for insertion into the vascular system. When inflated by circulating heat exchange fluid, the billows created by the pleating of the plastic sheet increases the surface area for heat exchange between the heat exchange fluid flowing in the catheter body and blood or other body fluid in heat exchange proximity within the interior passageway.

In another embodiment, as illustrated in FIG. **19**, a heat transfer catheter **420** may have a catheter body **422** formed as a blood channeling sleeve forming an inner passageway **423** with a heat exchanger such as a heat exchange balloon catheter **424** positioned within the inner passageway **423**. The heat exchanger may be any suitable heat exchanger, but in the embodiment shown the heat exchanger is a heat transfer balloon catheter, for example the type described in the previous sections or depicted in FIG. **17**B or FIG. **24**A below. The heat exchanger should be suitably sized and configured to provide sufficient heat exchange capabilities but allow adequate flow of fluid through the inner passageway.

The blood channeling sleeve has a proximal section **426** having a proximal opening **428**. The wall of the sleeve in the proximal section may additionally form orifices **430** to further enhance perfusion of fluid from the surrounding body portion into the inner passageway.

The sleeve further has an intermediate section **432**. The wall of the sleeve in the intermediate section is generally solid so that it generally will not permit fluid to exit the inner passageway through the wall of the sleeve in the intermediate section. The wall of the sleeve in the intermediate and indeed throughout its length, may be formed of a material with thermal insulation properties to thermally insulate fluid within the inner passageway from the tissue such as blood outside of the inner passageway. Thus fluid entering the inner passageway at the proximal section will be channeled through the intermediate section to the distal section **434** of the blood channeling sleeve.

The distal section **434** of the blood channeling sleeve has a distal opening **436**. Further, the wall of the blood channeling sleeve at the distal section may form orifices **438** that further enhance the flow of fluid out of the inner passageway and into the surrounding body portion such as a blood vessel. The distal end of the sleeve **436** may be proximal of the distal end of the heat exchanger **440**, may be co-extensive with the end of the heat exchanger (not shown) or may extend distal of the heat exchanger as is shown in FIG. **26**.

Additionally, there may be a central working lumen **442** that extends from the proximal end of the catheter shaft outside the patient's body to the distal end of the catheter shaft **443**. The central lumen may extend past the distal end of the heat exchange balloon or even past the distal end of the sleeve. The working lumen may be used to accommodate a guide wire or to inject dye or insert a microcatheter for additional procedures such as lysing a clot or performing injections through the microcatheter or any of the other uses for the working lumen as described above, particularly in reference to the working lumen shown in FIG. **17**. It will readily be appreciated that any of the above uses of the working lumen may be performed before, after, or even during the cooling of blood within the blood channeling sleeve. It may be one advantage of a catheter of the invention having a working lumen that the working lumen may be used for any of the above purposes at the same time that cooling is taking place and without inhibiting the cooling function of the catheter.

In use, the heat transfer catheter is placed in a fluid containing body, for example, as illustrated in FIG. **19**, the arterial system. The proximal end of the blood channeling sleeve may be, for example, located in the descending aorta **446**. The distal end of the catheter body is positioned as desired, in the case illustrated, in the left common carotid artery **448**, which delivers blood to the brain. The pressure differential between the aorta at the level of the proximal end of the sleeve and the left common carotid artery at the distal end of sleeve is sufficient to cause blood to flow through the sleeve, into left common carotid artery and thence to the brain. In the case illustrated, blood enters the inner passageway of the blood channeling sleeve located in the aorta, and travels through the inner passageway and in heat exchange proximity with the heat transfer balloon **424** in which heated or cooled heat exchange fluid is circulating. The blood is thus heated or cooled. The heated or cooled blood is then channeled out the distal end of the inner passageway where it flows into the left common carotid artery. If the heat exchanger is cooling the blood, cooled blood would thus be directed into the left common carotid and bath the brain in cooled blood. This, in turn, if maintained for a sufficient length of time, may result in regional cooling of the brain tissue with the advantages of that condition noted above.

It should be noted that the placement of the proximal opening of the blood channeling sleeve **423** down the descending aorta some distance from the aortic arch **447** will provide for a longer path for the blood to travel over the heat exchange balloon catheter in reaching the right common carotid than would be the case if blood were captured and directed through the inner passageway by a blood channeling sleeve located entirely within the left common carotid artery. This longer flow path provides for increased cooling effect relative to the shorter path. Also, the placement of the blood channeling sleeve at least partially in the aorta provides for the use of a larger heat exchanger, for example a

heat exchange balloon of greater diameter, than would be possible if the heat exchange portion of the catheter body was located in the right common carotid artery since the aorta is significantly larger in diameter than the right common carotid artery.

The distal section **434** of the blood channeling sleeve may also form a relatively tight fit around the blood vessel in which it is located. In this way, the pressure differential between the proximal and distal end of the sleeve is maximized, and essentially all the blood flowing from, for example, the aorta to the carotid artery passes through the inner passageway and is heated or cooled by the heat exchanger. The wall of the blood channeling sleeve may form an occlusive shoulder to facilitate the sealing of the artery. The heat exchanger is, for example, a heat transfer balloon that holds the walls of the catheter body extended, and the heat exchange balloon has fins or the like that will permit significant blood flow between the heat exchange balloon fins and between the inner walls of the inner passageway and the balloon, most if not all the blood entering the right common carotid artery would pass over the heat exchanger and thus is treated by heating or cooling.

Another embodiment of the heat transfer catheter of the invention is illustrated in FIG. **20**. The catheter **450** may be provided with a blood channeling sleeve **452** for the receipt and direction of body fluid such as blood. The sleeve may be essentially funnel shaped, having a distal region **454** that is significantly larger in diameter than its distal region **456**. In this manner, the exterior surface of the blood channeling sleeve may form an occlusive shoulder that may be pressed or rest against appropriate anatomical structures such as the interior of the artery in question, so that most or virtually all of the blood entering the artery in question is directed through the interior passageway **464** of the blood channeling sleeve before entering the artery. In the example illustrated, the artery into which the catheter body is inserted is the left common carotid artery, but it may be readily appreciated by those of skill in the art that the distal portion of the blood channeling sleeve may be configured for similar placement in other desired locations.

The distal region may be elongate with a substantially cylindrical shape and terminate in a distal opening **458**. Likewise, the proximal region may have a proximal opening **460** which may have a valve **462** for opening or closing the proximal opening or otherwise controlling entrance of the blood to the interior passageway **464** within the catheter body.

The interior of the proximal region **454** contains a heat exchanger. The heat exchanger depicted is a series of spiral fins **466** which may contain contains heat transfer balloons or balloon lobes for circulating heat transfer fluid. Alternatively the fins may be other types of heating or cooling mechanisms such as electric resistance heaters.

The heat transfer catheter may be provided with a catheter shaft **468** which may be provided with a working lumen **470** which may extend out of the patient's body when the heat exchange catheter is in place, and thus provide for the injection of drugs, fluoroscopic dye, or the like, and may accommodate a guide wire **472** for the placement of the heat transfer catheter. The shaft may also have channels (not shown) for the flow of heat transfer fluid, or contain electrical wires (not shown) to connect to the heat exchangers or sensors (also not shown) on the catheter.

In use, the heat transfer catheter **450** is placed in the desired body location. In the illustration of FIG. **20** the catheter is placed so that the proximal portion of the blood channeling sleeve **454** is within the aorta **474** and the distal portion **456** is within the left common carotid artery **476**. Blood flows down the aorta (illustrated with the arrows labeled "F") and may enter the proximal opening **460** of the catheter body if the valve **462** is open. The pressure differential between the blood in the aorta and the blood in the left common carotid is sufficient to cause the blood to flow up the inner passageway. As the blood flows up the inner passageway it passes in heat exchange proximity with the heat exchange fins **466** and is heated or cooled. The heated or cooled blood is channeled into the left common carotid by the blood channeling sleeve, and ultimately the heated or cooled blood baths the brain. If maintained for a sufficient length of time this may result in regionally heating or cooling of the brain.

Another embodiment of the heat transfer catheter of the invention is illustrated in FIG. **21**. The catheter **490** illustrated in that drawing is provided with a blood channeling sleeve **492** that is configured for placement in the blood vessels of the patient's body, for example the main arteries leading to the brain region **494**. The blood channeling sleeve is essentially cylindrical in shape, but may have a slightly enlarged proximal section **496** that creates a shoulder in the catheter body that may act as an occlusive shoulder **498** when the blood channeling sleeve is placed in an artery, such as an artery branching off the coronary arch.

The blood channeling sleeve is shaped as a tube and forms an inner passageway **500** that extends from the proximal section **496** that begins with a proximal opening **502** to the distal end which terminates at a distal opening. **504**. A heat exchanger such as a fined balloon heat exchange catheter **506** as described and illustrated in FIGS. **17**B and **24**A is located in the catheter body and may be contained entirely within the inner passageway **500** of the sleeve. The fins **508** provide for added heat transfer surface relative to a cylindrically shaped heat exchange balloon, and also create flow channels between the fins for the flow of blood from the proximal opening, over and between the fins of the heat exchange balloon, and out the distal end of the inner passageway. A catheter shaft **509** may also be provided as described in conjunction with the other embodiments described above.

FIGS. **21**B–D illustrate the operation of a control system to regulate the opening and closing of a valve assembly **460** that may be formed along any section of the sleeve **492** such as at the proximal opening **502** in order to control the flow of blood within the inner passageway **500**. For example, a bi-leaflet valve **510** may be positioned at the proximal opening of the sleeve **492** around the catheter shaft. The valve **510** may have at least one closed position as shown in FIG. **21**B and at least one open position as shown in FIG. **21**C. Other valves such as one-way valves may be selected for the catheter body, and the valve may be opened and closed to a variable degree to control the amount of fluid passing through the sleeve at selected points in time.

The valve **510** may be synchronously opened and/or closed in accordance with the heartbeat of a patient as illustrated by the graph of FIG. **21**D. Because aortic blood flow (L/min) is pulsatile and fluctuates at different time intervals during the heartbeat cycle, a valve may be selectively opened when a relatively large amount of blood is released from the heart. At the same time, the valve may be selectively closed to retain the blood within the inner passageway **500** when the blood flow is slower. Alternatively, the valves may be controlled to cause blood to flow more slowly through the inner passageway to allow for all the blood passing in to the artery distal of the catheter body flows slowly over the head exchanger for maximum heating or cooling.

As described above, a catheter control unit may simultaneously monitor body conditions or sensed stimuli such as the heart rate, temperature at various locations, and pressure within the apparatus or within the patient. When the valve **510** is in a closed position (FIG. **21**B), blood or fluid is retained within the inner passageway **500** and effectively cooled by the internally positioned heat exchanger **506**. A valve in a closed position may prevent or minimize backflow of cooled fluid away from the brain. After the blood is allowed to cool, when the heart begins to send more blood in the direction of the heat transfer catheter, the valve may be activated to assume an open position (FIG. **21**C) to allow the cooled blood to be pushed out of the confined cooling area by the relatively warmer incoming blood. When the pressure or surge of blood from the heart subsides thereafter, the valve **510** may again close, and this cooling and pumping cycle continues repeatedly until the desired level of regional hypothermia in the brain is achieved. FIG. **21** D is a graphic representation of the cycle just described.

Although many of the embodiments of the invention described thus far are illustrated as either a cooling apparatus or a heating apparatus, it should be understood that any combination of these variations may form a series or a network of thermoregulating devices. For example, as shown in FIG. **22**, a heat exchange catheter **520** includes a heat transfer balloon **524** with a plurality of collapsible cooling fins **522** placed in the aortic **526** region. A suitable heat transfer balloon catheter with fins has been previously described. The heat exchange catheter may be provided with a catheter shaft **528**. The heat exchange catheter may have a heating element **530** formed at a different location along the catheter shaft than the cooling balloon **524**. The shaft **528** may include a pair of longitudinal fluid paths (not shown) for circulating hot heat transfer medium to the heating element as well as an additional pair of fluid paths (not shown) that circulate cold heat transfer medium to the cooling balloon **522**. Alternatively, the heating fin **530** may include a resistance heater or other heating elements known in the art. In the case of a resistance heating element, electrical current may pass through wires withing the shaft (not shown) to the heat-generating element.

The cooling balloon **522** may include an insulated underside **534**. Blood flowing in a certain direction, for example to the brain region, may thus be preferentially cooled relative to blood flowing to other areas of the patient's body, for example to the lower body. In the example illustrated in FIG. **22**, the heat transfer region includes a curved cooling balloon that is thermally insulated along the inner radius of its curvature and thermally conductive along its outer radius of its curvature. The cooling balloon may be placed in the aortic arch. Blood is pumped by the heart into the aorta (indicated by arrows F) and some flows over the top surface **523** of the cooling balloon **522** in heat exchange proximity to the balloon surface. This blood is cooled, and the cool blood then flows naturally to the brain region. Blood flowing past the inner, insulated curvature of radius **525** is not cooled, and thus blood of normal temperature flows down the aorta and to the lower body. It may be noted that, in the example illustrated, cool blood flows to the brain region through all of the arteries extending from the aortic arch without the need to cannulate each of those arteries. In such a configuration, it is also unnecessary to provide the heat transfer catheter with a blood channeling sleeve since the directional cooling is obtained without using the catheter to direct the cool blood to specific arteries.

As described, heating and cooling mechanisms may be formed at various locations along the shaft **528** of the heat transfer catheter **524**. Alternatively, multiple heating and cooling catheters may be used in combination or cooperatively. As previously described, a common catheter control unit may monitor and control multiple devices individually or collectively, and may be responsive to one or more sensors (not shown) such as pressure sensors or temperature sensors.

Another aspect of the invention is illustrated in FIG. **23** whereby heated or cooled blood may be directed to a specific location such as a tumor, or organ such as the heart, through a relatively small vessel. A heat transfer catheter **550** is provided having a blood channeling sleeve **552**, which sleeve has a proximal opening **554** and a distal end section **552**. A heat exchanger **558** which may be, for example, a finned heat transfer balloon as described above, is located within the blood channeling sleeve. The heat transfer catheter has a catheter shaft **560**, which extends from at least the interior of the blood channeling sleeve to a distal end **562**. The distal section of the sleeve is seated around the catheter shaft **564**. The catheter shaft **560** has a perfusion lumen **566** extending between blood inlet orifices **568**, **570** formed in the catheter shaft at a point within the blood channeling above, and the distal end **562** of the shaft. The blood inlet orifices provide fluid communication between the perfusion lumen and the interior **572** of the blood channeling sleeve.

In use, the heat transfer catheter **560** is placed into a patient's vasculature, for example the aorta **574**, and is positioned so that the distal end **562** of the catheter shaft **560** in a desired location, for example, in the coronary ostium. The pressure differential between the blood in the aorta at the proximal end of the blood channeling sleeve **552** and the distal end **566** of the catheter shaft causes blood to flow through the proximal opening of the sleeve, through **554** the inner passageway and in heat transfer proximity to the heat exchanger at which time the blood will be heated or cooled, and into the blood inlet orifices through the central lumen of the catheter shaft and out the distal tip of the central lumen **578**. In this way, a strewn of heated or cooled blood may be directed to a specific organ or tissue, for example the heart or tumor, and bath that organ or tissue in the heated or cooled blood. If a sufficient portion of the organ or tissue's blood supply is treated in this manner for a sufficient time, regional heating or cooling of the organ or tissue in question will result.

The central lumen may extend from the distal tip **578** to a proximal opening outside the body. In this way the central lumen may function as a working lumen for all applications as previously described including angiography and acting as a guide catheter for angioplasty. The central or working lumen may be sized to function as a guide catheter and allow simultaneous insertion of an angioplasty catheter and infusion of cold blood through the central or working lumen.

An alternative construction to the heat exchange balloon as illustrated in FIG. **17** is shown in FIG. **24**A wherein the heat exchange region is formed using a series of three collapsible balloon lobes **902**, **904**, **906** located around a central collapsible lumen **908**. A proximal shaft **910** is formed having two channels, an inlet channel **912** and an outlet channel **914**. The interior of the shaft is divided into two lumens by webs **916**, **917**, but the lumens do not occupy equal portions of the interior of the shaft. The inlet channel occupies about ⅓ of the circumference of the interior, the outlet channel occupies about ⅔ of the circumference of the interior for reasons that will be explained below.

At the heat exchange region of the catheter, a transition **915** is formed between the shaft **910** and the tube **911** forming the central collapsible lumen **908**. The outlet chan-

nel is plugged **917**, the tube **911** is affixed over the shaft **910** by, for example gluing, at the transition **915**, and the shaft ends with the tube (not shown). In this way, as shown in FIG. **24**C, the inlet channel in this portion of the catheter occupies the entire circumference of the shaft. At the distal end of the balloon, inlet orifices **918**, **920**, **922** are formed between the inlet channel and the three collapsible balloons. At the proximal end of the heat exchange region, outlet orifices **924**, **926**, **928** are formed between the interior of each balloon and the outlet channel in the shaft. As may be seen in FIG. **30**D, the configuration of the outlet channel is such that communication with the interior of each of the three balloons is possible.

As may be appreciated, heat exchange fluid (not shown) may flow down the inlet channel in the shaft **912**, continue down lumen **908** to the distal end of the heat exchange region, exit the lumen through the inlet orifices **918**, **919**, **920** to the interior lumens of the balloon lobes **919**, **921**, **923**, travel back down each of the three balloons and re-enter the shaft through the outlet orifices **924**, **926**, **928** and then down the outlet channel **914** toward the proximal end of the catheter. In this way heat exchange fluid may be circulated through the three balloons to add heat to the blood flowing in heat transfer proximity to the balloons if the heat exchange fluid is warmer than the blood, or to remove heat from the blood if the heat exchange fluid is cooler than the blood. The material from which the balloons are made is made of a material that will permit significant thermal exchange between the heat exchange fluid on the interior of the balloon and the body fluid such as blood flowing in heat exchange proximity to the surface of the balloon. One such appropriate material is very thin plastic material, which may also be made strong enough to withstand the pressure necessary for adequate flow of the heat exchange fluid.

It may also readily be appreciated that the same heat exchange balloon of the type described here and in conjunction with FIG. **17** may be used to add heat to the blood stream or remove heat from the blood stream depending on the relative temperature of the heat exchange fluid and the blood flowing in heat exchange proximity to the balloon. That is, the same device at the same location may be used alternately to add or to remove heat merely by controlling the temperature of the heat exchange fluid within the device.

A heat exchange device may also be supplied as a kit comprising the heat exchange device and a set of instruction for using the heat exchange device. The heat exchange device may comprise, for example, a heat exchange catheter as described in this application. The instructions for use will generally instruct the user to insert the heat exchange device into a body fluid containing region and to establish the temperature of the heat exchange device to affect the temperature of the body fluid. The instructions for use may direct the user to heat or cool the body fluid to achieve any of the purposes described in this application.

While all aspects of the present invention have been described with reference to the aforementioned applications, this description of various embodiments and methods shall not be construed in a limiting sense. The aforementioned is presented for purposes of illustration and description. It shall be understood that all aspects of the invention are not limited to the specific depictions, configurations or relative proportions set forth herein which depend upon a variety of conditions and variables. The specification is not intended to be exhaustive or to limit the invention to the precise forms disclosed herein. Various modifications and insubstantial changes in form and detail of the particular embodiments of the disclosed invention, as well as other variations of the invention, will be apparent to a person skilled in the art upon reference to the present disclosure. It is therefore contemplated that the appended claims shall cover any such modifications or variations of the described embodiments as falling within the true spirit and scope of the invention.

What is claimed is:

1. A method for lessening the severity of damage to neural tissue located within the body of a mammalian patient after said neural tissue has become ischemic or has been otherwise affected by a disease, disorder or trauma which can cause subsequent damage, infraction, hemorrhage or necrosis of said tissue, said method comprising the steps of:

A. selecting a portion of the body comprising the brain which contains the tissue, said portion of the body receiving a flow of a body fluid;

B. providing a heat exchange catheter device which comprises; i) an elongate, flexible catheter having a proximal end, a distal end, and an insertion portion for insertion into a patient's body ii) at least one fluid lumen through which a thermal exchange fluid may be circulated and iii) a heat exchanger located a first location on the catheter along a length of said insertion portion which is less than the entire length of said insertion portion, said heat exchanger being operative to exchange heat between body fluid which flows in heat exchange proximity to said heat exchanger and thermal fluid which is circulated through said catheter;

C. inserting the catheter into a fluid-containing body structure of the patient and positioning the catheter such that fluid flowing through the body structure will pass in heat exchange proximity to the heat exchanger before reaching the selected body portion;

D. circulating a heat portion exchange fluid through the fluid lumen of the catheter device, such that body fluid will pass in heat exchange proximity to the heat exchanger, said heat exchange fluid being at a temperature other than the body fluid, whereby the temperature of the body fluid will be altered, and will subsequently flow to said neural tissue;

E. maintaining the catheter in said position and with the heat transfer fluid at said temperature for a sufficient time to alter the temperature of the neutral tissue, and;

F. maintaining the selected portion of the body in Step A at a temperature different than that of the rest of the patient's body by wrapping at least a portion of the patient's body below the head in warming blankets.

2. The method of claim **1** wherein the fluid containing body structure recited in Step C is a blood vessel and the body fluid recited in Step A is blood.

3. The method of claim **2** wherein the blood vessel is an artery.

4. The method of claim **2** wherein the blood vessel is a vein.

5. The method of claim **1** wherein the catheter device provided in Step B further comprises iv) a blood channeling sleeve formed about a segment of said catheter whereon said heat exchanger is located such that a blood flow space exists between said catheter and said blood channeling sleeve, said blood channeling sleeve having a blood inlet located proximal to at least a portion of the heat exchanger and a blood outlet located distal to at least a portion of said heat exchanger, and wherein the catheter is positioned in Step C such that blood which exits the blood outlet will flow to a blood vessel which perfuses said neural tissue.

6. The method of claim **5** wherein the catheter is further positioned in Step C such that the blood outlet is within a

first blood vessel which leads to said neural tissue and the blood inlet is within a second blood vessel, blood from the second blood vessel being thereby channeled through the blood channeling sleeve in heat exchanging proximity to the heat exchanger, and subsequently flowing into said first blood vessel to cool said neural tissue.

7. The method of claim **6** wherein the neural tissue is located in the brain and the first blood vessel is selected from the group consisting of:

right common carotid artery;

left common carotid artery;

innominate artery;

right internal carotid artery; and,

left internal carotid artery.

8. The method of claim **7** wherein the second blood vessel is the aorta.

9. The method of claim **8** wherein the blood inlet of the blood channeling sleeve is located within the descending aorta.

10. The method of claim **6** wherein at least a portion of the blood channeling sleeve is located in said first blood vessel, and has an outer diameter that is approximately as large as the luminal diameter of the first blood vessel other than through the blood flow space between the catheter and the blood channeling sleeve.

11. The method of claim **10** wherein the first blood vessel is a branch vessel which emanates from the arch of the aorta and the second blood vessel is the aorta.

12. The method of claim **6** wherein at least a portion of the blood channeling sleeve is located in said first blood vessel, said blood channeling sleeve having a shoulder between said blood inlet and said blood outlet, said shoulder sized to cause at least a partial occlusion between said first blood vessel and said second blood vessel to prevent blood flowing from said second blood vessel to said first blood vessel other than through said blood channeling sleeve.

13. The method of claim **1** further comprising the steps of:

G. providing a second heat exchange catheter device which comprises; 1) an elongate, flexible catheter having a proximal end and a distal end, ii) a heat exchanger located at a first location on the catheter, said heat exchanger being operative to exchange heat between blood which flows in heat exchanging proximity to said heat exchanger and the heat exchanger;

H. inserting the second catheter into the patient's vasculature and positioning it at a second location such that which has cooled the neural tissue in Step D of the method will subsequently flow in heat exchange proximity to the heat exchanger of the second catheter; and,

I. adding heat to said blood.

14. The method of claim **1** wherein the catheter device provided in Step A further comprises a wording lumen and wherein the positioning of the catheter in Step C is accomplished by advancing the catheter over a previously inserted guide wire such that the guide wire extends through the working lumen of the catheter.

15. The method of claim **1** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

G. infusing a medicament through the working lumen of the catheter to deliver said medicament to the neural tissue.

16. The method of claim **15** wherein the medicament is selected from the group of medicaments consisting of:

a thrombolytic agent;

an anticoagulant;

neuro-protectant;

a barbiturate;

a anti-seizure agent;

an oxygenated perfusate;

a vaso-dilator;

an agent which prevents vaso-spasm;

an agent which inhibits platelet activation; and,

an agent which deters the adhesion of platelets.

17. The method of claim **1** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

G. infusing a radiographic contrast agent through the working lumen of the catheter to permit imaging in the area of said neural tissue.

18. The method of claim **1** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

G. passing a therapeutic apparatus through the working lumen of the catheter and using such therapeutic apparatus to perform a therapeutic task.

19. The method of claim **18** wherein the therapeutic apparatus passed through the working lumen of the catheter in Step G is selected from the group of therapeutic apparatus consisting of:

an angioplasty catheter;

an embolectomy catheter;

an occlusion member delivering catheter;

an electro-cautery device; and,

a microcatheter.

20. The method of claim **1** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

G. passing a diagnostic device through the working lumen of the catheter and using such diagnostic device to perform a diagnostic procedure.

21. The method of claim **20** wherein the diagnostic device is selected from the group consisting of:

an angiographic catheter;

a sensor.

22. The method of claim **1** wherein the neural tissue is brain tissue which has become ischemic or has suffered hypoxic insult due to a stroke.

23. The method of claim **1** wherein the neural tissue is brain tissue which has suffered hypoxic insult due to cardiac arrest.

24. A method for lessening the severity of damage to neural tissue located within the body of a mammalian patient after said neural tissue has become ischemic or has been otherwise affected by a disease, disorder or trauma which can cause subsequent damage, infarction, hemorrhage or necrosis of said tissue, said method comprising the steps of:

A. selecting a portion of the body which contains the tissue, said portion receiving a flow of a body fluid;

B. providing a heat exchange catheter device which comprises; i) an elongate, flexible catheter having a proximal end, a distal end, and an insertion portion for insertion into a patient's body ii) at least one fluid lumen through which a thermal exchange fluid may be circulated and iii) a heat exchanger located a first location on the catheter along a length of said insertion portion which is less than the entire length of said insertion portion, said heat exchanger being operative

to exchange heat between body fluid which flows in heat exchange proximity to said heat exchanger and the thermal fluid which is circulated through said catheter;

C. inserting the catheter into a fluid-containing body structure of the patient and positioning the catheter such that fluid flowing through the body structure will pass in heat exchange proximity to the heat exchanger before reaching the selected body portion;

D. circulating a heat exchange fluid through the fluid lumen of the catheter device, such that body fluid will pass in heat exchange proximity to the heat exchanger, said heat exchange fluid being at a temperature other than the body fluid, whereby the temperature of the body fluid will be altered, and will subsequently flow to said neural tissue;

E. maintaining the catheter in said position and with the heat transfer fluid at said temperature for sufficient time to alter the temperature of the neural tissue;

F. providing a second heat exchange catheter device which comprises; 1) an elongate, flexible catheter having a proximal end and a distal end, ii) a heat exchanger located at a first location on the catheter, said heat exchanger being operative to exchange heat between blood which flows in heat exchanging proximity to said heat exchanger and the heat exchanger;

G. inserting the second catheter into the patient's vasculature and positioning it at a second location such that blood which has cooled the neural tissue in Step D of the method will subsequently flow in heat exchange proximity to the heat exchanger of the second catheter; and,

H. adding heat to said blood.

25. The method of claim **24** wherein the fluid containing body structure recited in Step C is a blood vessel and the body fluid recited in Step A is blood.

26. The method of claim **25** wherein the blood vessel is an artery.

27. The method of claim **25** wherein the blood vessel is a vein.

28. The method of claim **24** wherein the body portion in Step A is the brain.

29. The method of claim **28** further comprising the step of:

I. maintaining the selected portion of the body in Step A at a temperature different than that of the rest of the patient's body.

30. The method of claim **29** wherein Step I comprises wrapping at least a portion of the patient's body below the head in warming blankets.

31. The method of claim **24** wherein the catheter device provided in Step B further comprises iv) a blood channeling sleeve formed about a segment of said catheter whereon said heat exchanger is located such that a blood flow space exists between said catheter and said blood channeling sleeve, said blood channeling sleeve having a blood inlet located proximal to at least a portion of the heat exchanger and a blood outlet located distal to at least a portion of said heat exchanger, and wherein the catheter is positioned in Step C such that blood which exists the blood outlet will flow to a blood vessel which perfuses said neural tissue.

32. The method of claim **31** wherein the catheter is further positioned in Step C such that the blood outlet is within a first blood vessel which leads to said neural tissue and the blood inlet is within a second vessel, blood from the second blood vessel being thereby channeled through the blood channeling sleeve in heat exchanging proximity to the heat exchanger, and subsequently flowing into said first blood vessel to cool said neural tissue.

33. The method of claim **32** wherein the neural tissue is located in the brain and the first blood vessel is selected from the group consisting of:

right common carotid artery;

left common carotid artery;

innominate artery;

right internal carotid artery; and,

left internal carotid artery.

34. The method of claim **33** wherein the second blood vessel is the aorta.

35. The method of claim **34** wherein the blood inlet of the blood channeling sleeve is located within the descending aorta.

36. The method of claim **32** wherein at least a portion of the blood channeling sleeve is located in said first blood vessel, and has an outer diameter that is approximately as large as the luminal diameter of the first blood vessel such that blood is substantially prevented from entering the first blood vessel other than through the blood flow space between the catheter and the blood channeling sleeve.

37. The method of claim **36** wherein the first blood vessel is a branch vessel which emanates from the arch of the aorta and the second blood vessel is the aorta.

38. The method of claim **32** wherein at least a portion of the blood channeling sleeve is located in said first blood vessel, said blood channeling sleeve having a shoulder between said blood inlet and said blood outlet, said shoulder sized to cause at least a partial occlusion between said first blood vessel and said second blood vessel to prevent blood flowing from said second blood vessel to said first blood vessel other than through said blood channeling sleeve.

39. The method of claim **24** wherein the catheter device provided in Step A further comprises a working lumen and wherein the positioning of the catheter in Step B is accomplished by advancing the catheter over a previously inserted guide wire such that the guide wire extends through the working lumen of the catheter.

40. The method of claim **24** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

I. infusing a medicament through the working lumen of the catheter to deliver said medicament to the neural tissue.

41. The method of claim **40** wherein the medicament is selected from the groups of medicaments consisting of:

a thrombolytic agent;

an anticoagulant;

a neuro-proctectant;

a barbiturate;

a anti-seizure agent;

an oxygenated perfusate;

a vaso-dilator;

an agent which prevents vaso-spasm;

an agent which inhibits platelet activation; and,

an agent which deters the adhesion of platelets.

42. The method of claim **24** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

I. infusing a radiographic contrast agent through the working lumen of the catheter to permit imaging in the area of said neural tissue.

43. The method of claim **24** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

I. passing a therapeutic apparatus through the working lumen of the catheter and using such therapeutic apparatus to perform a therapeutic task.

44. The method of claim **43** wherein the therapeutic apparatus passed through the working lumen of the catheter in Step I is selected from the group of therapeutic apparatus consisting of:

an angioplasty catheter;

an embolectomy catheter;

an occlusion member delivering catheter;

an electro-cautery device; and,

a microcatheter.

45. The method of claim **24** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

I. passing a diagnostic device through the working lumen of the catheter and using such diagnostic device to perform a diagnostic procedure.

46. The method of claim **45** wherein the diagnostic device is selected from the group consisting of:

an angiographic catheter and

a sensor.

47. The method of claim **24** wherein the neural tissue is brain tissue which has become ischemic or has suffered hypoxic insult due to a stroke.

48. The method claim **24** wherein the neural tissue is brain tissue which has suffered hypoxic insult due to cardiac arrest.

49. A method for lessening the severity of damage to neural tissue located within the body of a mammalian patient after said neural tissue has become ischemic or has been otherwise affected by a disease, disorder or trauma which can cause subsequent damage, infarction, hemorrhage or necrosis of said tissue, said method comprising the steps of:

A. selecting a portion of the body containing the tissue, which portion receives a flow of a body fluid;

B. providing a heat exchange catheter device which comprises; i) an elongate, flexible catheter having a proximal end, a distal end, and an insertion portion for insertion into a patient's body ii) at least one fluid lumen through which a thermal exchange fluid may be circulated iii) a heat exchanger located a first location on the catheter along a length of said insertion portion which is less than the entire length of said insertion portion, said heat exchanger being operative to exchange heat between body fluid which flows in heat exchange proximity to said heat exchanger and the thermal fluid which is circulated through said catheter and iv) a blood channeling sleeve formed about a segment of said catheter whereon said heat exchanger is located such that blood flow space exists between said catheter and said blood channeling sleeve, said blood channeling sleeve having a blood inlet located proximal to at least a portion of the heat exchanger and a blood outlet located distal to at least a portion of said heat exchanger;

C. inserting the catheter into fluid-containing body structure of the patient and positioning the catheter such that fluid flowing through the body structure will pass in heat exchange proximity to the heat exchanger before reaching the selected body portion and wherein the catheter is positioned such that blood which exits the blood outlet will flow to a blood vessel which perfuses said neural tissue;

D. circulating a heat exchange fluid through the fluid lumen of the catheter device, such that body fluid will pass in heat exchange proximity to the heat exchanger, said heat exchange fluid being at a temperature other than the body fluid, whereby the temperature of the body fluid will be altered, and will subsequently flow to said neural tissue;

E. maintaining the catheter in said position and with the heat transfer fluid at said temperature for a sufficient to alter the temperature of the neural tissue.

50. The method of claim **49** wherein the fluid containing body structure recited in Step C is a blood vessel and the body fluid recited in Step A is blood.

51. The method of claim **50** wherein the blood vessel is an artery.

52. The method of claim **50** wherein the blood vessel is a vein.

53. The method of claim **49** wherein the body portion in Step A is the brain.

54. The method of claim **53** further comprising:

F. maintaining the selected portion of the body in Step A at a temperature different than that of the rest of the patient's body.

55. The method of claim **54** wherein Step F comprises wrapping at least a portion of the patient's body below the head in warming blankets.

56. The method of claim **49** wherein the catheter is further positioned in Step B such that the blood outlet is within a first blood vessel which leads to said neural tissue and the blood inlet is within a second blood vessel, blood from second blood vessel being thereby channeled through the blood channeling sleeve in heat exchanging proximity to the heat exchanger, and subsequently flowing into said first blood vessel to cool said neural tissue.

57. The method of claim **56** wherein the neural tissue is located in the brain and the first blood vessel is selected from the group consisting of:

right common carotid artery;

left common carotid artery;

innominate artery;

right internal carotid artery; and,

left internal carotid artery.

58. The method of claim **57** wherein the second blood vessel is the aorta.

59. The method of claim **58** wherein the blood inlet of the blood channeling sleeve is located within the descending aorta.

60. The method of claim **57** wherein at least a portion of the blood channeling sleeve is located in said first blood vessel, said blood channeling sleeve having a shoulder between said blood inlet and said blood outlet, said shoulder sized to cause at least a partial occlusion between said first blood vessel and said blood vessel to prevent blood flowing from said second blood vessel to said first blood vessel other than through said blood channeling sleeve.

61. The method of claim **56** wherein at least a portion of the blood channeling sleeve is located in said first blood vessel, and has an outer diameter that is approximately as large as the luminal diameter of the first blood vessel such that blood is substantially prevented from entering the first blood vessel other than through the blood flow space between the catheter and the blood channeling sleeve.

62. The method of claim **61** wherein the first blood vessel is a branch vessel which emanates from the arch of the aorta and the second blood vessel is the aorta.

63. The method of claim **49** further comprising the steps of:

F. providing a second heat exchange catheter device which comprises; i) an elongate, flexible catheter hav-

ing a proximal end and a distal end, ii) a heat exchanger located at first location on the catheter, said heat exchanger being operative to exchange heat between blood which flows in heat exchanging proximity to said heat exchanger and the heat exchanger;

G. inserting the second catheter into the patient's vasculature and positioning it at a second location such that blood which has cooled the neural tissue in Step D of the method will subsequently flow in heat exchange proximity to heat exchanger of the second catheter; and,

H. adding heat to said blood.

64. The method of claim **49** wherein the catheter device provided in Step A further comprises a working lumen and wherein the positioning of the catheter in Step B is accomplished by advancing the catheter over a previously inserted guide wire such that the guide wire extends through the working lumen of the catheter.

65. The method of claim **49** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

F. infusing a medicament through the working lumen of the catheter to deliver said medicament to the neural tissue.

66. The method of claim **65** wherein the medicament is selected from the group of medicaments consisting of:

thrombolytic agent;

an anticoagulant;

a neuro-protectant;

a barbiturate;

a anti-seizure agent;

an oxygenated perfusate;

a vaso-dilator;

an agent which prevents vaso-spasm;

an agent which inhibits platelet activation; and,

an agent which deters the adhesion of platelets.

67. The method of claim **49** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

F. infusing a radiographic contrast agent through the working lumen of the catheter to permit imagining in the area of said neural tissue.

68. The method of claim **49** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

F. passing a therapeutic apparatus through the working lumen of the catheter and using such therapeutic apparatus to perform a therapeutic task.

69. The method of claim **68** wherein the therapeutic apparatus passed through the working lumen of the catheter in Step D is selected from the group of therapeutic apparatus consisting of:

an angioplasty catheter;

an embolectomy catheter;

an occlusion member delivering catheter;

an electro-cautery device; and,

a microcatheter.

70. The method of claim **49** wherein the catheter device provided in Step A further comprises a working lumen and wherein the method further comprises the step of:

F. passing a diagnostic device through the working lumen of the catheter and using such diagnostic device to perform a diagnostic procedure.

71. The method of claim **70** wherein the diagnostic device is selected from the group consisting of:

an angiographic catheter;

a sensor.

72. The method of claim **49** wherein the neural tissue is brain tissue which has become ischemic or has suffered hypoxic insult due to a stroke.

73. The method of claim **49** wherein the neural tissue is brain tissue which has suffered hypoxic insult due to cardiac arrest.

* * * * *

US005562821A

United States Patent [19]

Gutierrez-Collazo

[11] Patent Number: 5,562,821

[45] Date of Patent: Oct. 8, 1996

[54] **FOAM FRACTIONATOR**

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[73] Assignee: **Commonwealth of Puerto Rico**, San Juan, Puerto Rico

[21] Appl. No.: **505,664**

[22] Filed: **Jul. 21, 1995**

[51] **Int. Cl.**[6] **C02F 1/24**

[52] **U.S. Cl.** **210/169**; 210/219; 210/221.1; 261/93; 119/263; 119/264

[58] **Field of Search** 210/169, 219, 210/221.1, 416.2; 261/93; 119/263, 264

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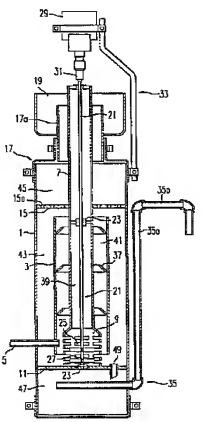
Attorney, Agent, or Firm—Oblon, Spivak, McClelland, Maier & Neustadt, P.C.

[57] **ABSTRACT**

A foam fractionator which can create a vortex is utilized to remove proteins from an aquatic environment by skimming. The vortex is created by a propeller arrangement located at the bottom of an internal chamber, centrally located within a main reaction chamber. Air sucked from the atmosphere by the vortex passes down through a central chamber and is dispensed outwardly into the main chamber where air bubbles form and rise to the surface. The air bubbles attract protein deposits which stick thereto which results in the formation of a protein-containing surface foam that is collected within a collection cup.

11 Claims, 4 Drawing Sheets



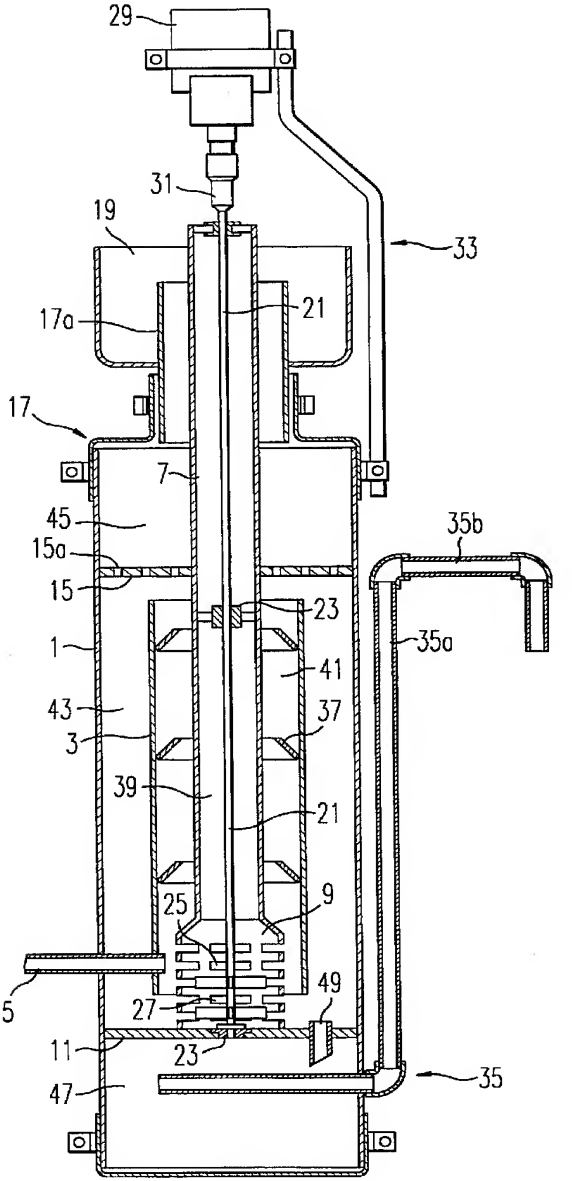

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FIG. 1

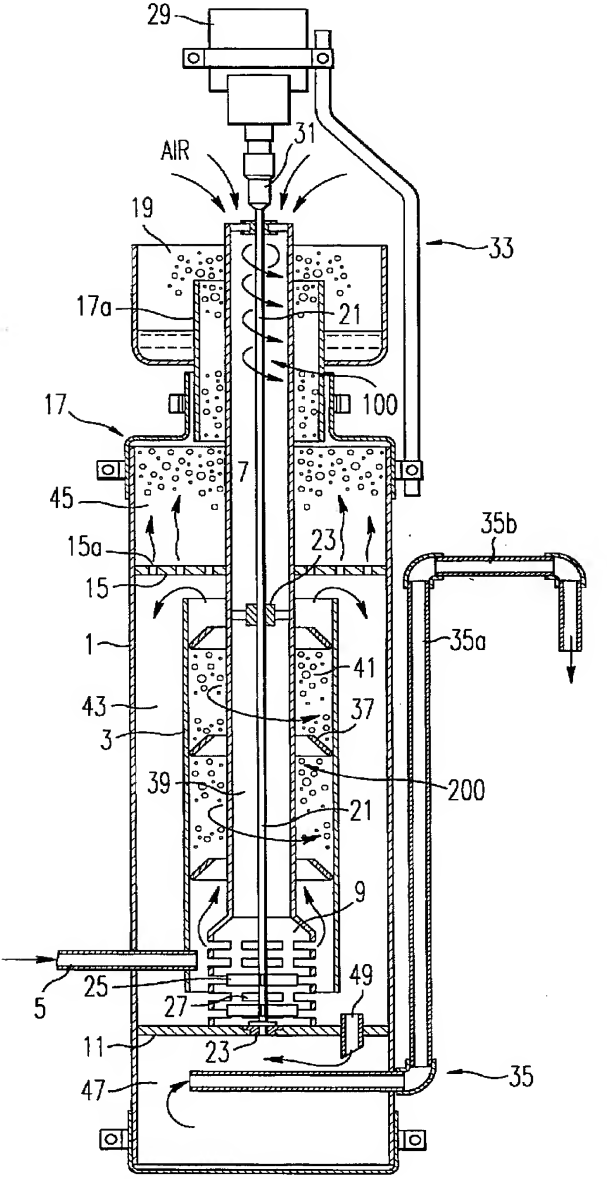
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FIG. 2

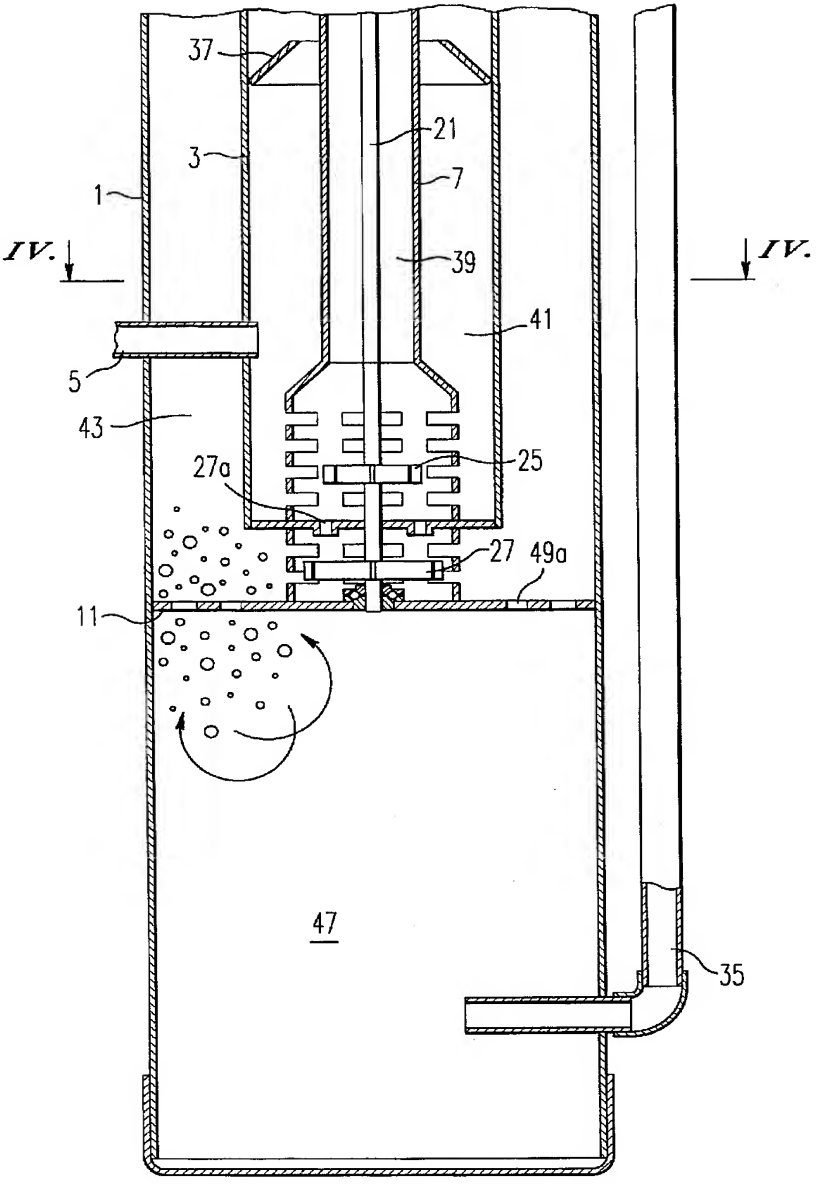

FIG. 3

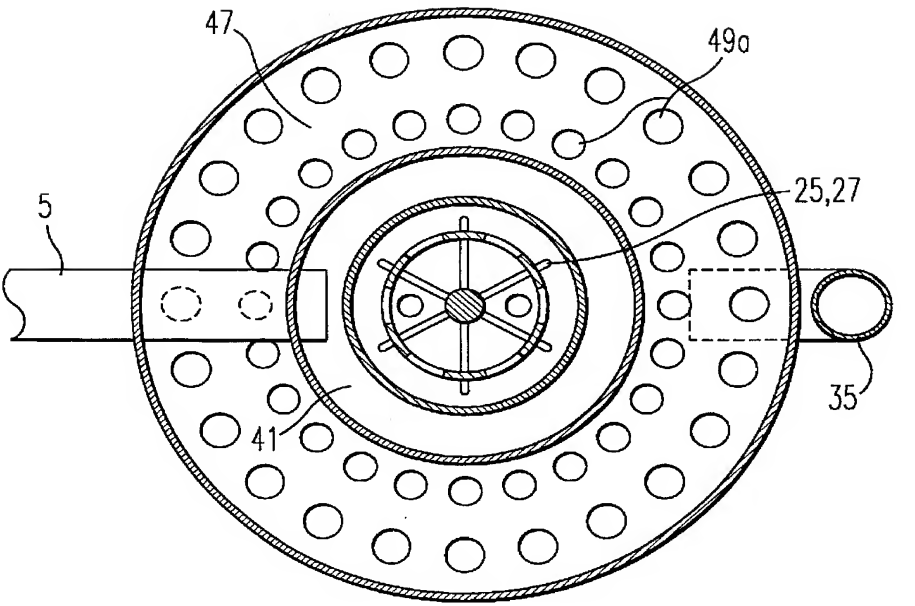

FIG. 4

FOAM FRACTIONATOR

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a foam fractionator such as a vortex foam fractionator which removes proteins from an aquatic environment by skimming. In the apparatus of the present invention, a vortex is created by propeller means located at the bottom of an internal chamber, centrally located within a main reaction chamber. Air sucked from the atmosphere by the vortex passes down through the central chamber and is dispensed outwardly into the main chamber where air bubbles form and rise to the surface. The air bubbles attract protein deposits which stick together resulting in the formation of a protein containing surface foam which is collected within a collection cup. The propeller means include a first propeller positioned within a central tube which forms an air vortex, and a second propeller which pumps air into descending water flow passing over an upper edge of the central pump tube.

2. Discussion of the Background

Filtration methods are utilized in both aquaculture and aquaristics and permit a user to keep a water quality level sufficiently high so as to duplicate an aquatic ecosystem and even achieve the reproduction of some species in captivity. These filtration methods can be divided into three general groups depending on their function. A first group involves mechanical filters which are used in many water filtration systems and function to trap and retain water-borne particles inside a media that can be discarded or washed and re-used once it is saturated. Examples of mechanical filters involve floss, sponges, sand filters and sub-micronic filters.

A second group of filtering systems is a biological-type filtering system. Since bacterial action occurs on all ecosystems to degrade organic and inorganic matter to less complex by-products and create in the process a more adequate environment for higher forms of life, several methods of water purification that utilize bacterial colonies to biodegrade other animals' waste have been developed. During this process, a delicate balance is achieved inside an artificial environment. Biological filters create a symbiotic relation between bacteria and the rest of the organisms that inhabit the system. An example of biological filter devices are under-gravel plates, wet/dry systems, etc.

A third group of filters involves chemical filters. These filters can basically absorb impurities dissolved in water and retain them inside a media. Chemical filters are not the same as mechanical filters which just absorb particles, chemical filters use electrochemical force to attract the impurities to themselves. Examples of chemical filters include activated carbon, de-ionizers, molecular absorption media and protein skimmers.

Protein skimmers basically involve three types of processes. These processes include a co-current protein skimmer, a counter-current protein skimmer and a venturi protein skimmer. These protein skimmers basically use the concept of mixing air with water to achieve a skimming action. That is, a protein skimmer is a chemical filtering device that works by using air bubbles for water purification.

In an artificial aquatic environment organic compounds, proteins among them, accumulate by the metabolic waste of animals and plants, the slow decay of matter, and the addition of food to the system. In nature, these compounds are bio-degraded, and utilized also by plants for their own metabolism. In a closed artificial environment, it is difficult

to prevent an accumulation of organic compounds capable of damaging the closed environment. As a result, partial water changes are needed to perform and maintain adequate water conditions. Even though bacterial action in plants can take care of much of the work to keep an aquarium system healthy, water changes are necessary nevertheless because bacteria and plants also produce their own waste that, although it is much less toxic to higher organisms, needs to be removed periodically.

Conventional protein skimmers have drawbacks in that they do not adequately prevent the buildup of waste including bacterial by-products in water that could be detrimental to the well being of a delicate organism and adversely affects the quality of the water.

SUMMARY OF THE INVENTION

An object of the present invention is to provide for an improved foam fractionator that works by utilizing air bubbles for water purification.

The fractionator of the present invention is capable of extracting organic compounds from an aquatic environment before they are attacked by bacterial action. This raises the quality of the system's water and prevents buildup of waste, including bacterial by-products, that could be detrimental to the well-being of delicate organisms. This also raises the dissolved oxygen in the water and by eliminating most of the bacterial intervention in the water management process which consumes plenty of oxygen, the concentration of this gas will go up.

In an aquatic system, organic molecules that dissolve in water generally have two extremes, one hydrophilic (attracted to water) and one hydrophobic (repels water). This characteristic makes these molecules rise to the interface of a water column. They are like little buoys that float with the hydrophilic side facing down to the water and the hydrophobic side facing toward the atmosphere. This type of molecule is known as a surfactant.

The fractionator of the present invention works by constantly mixing water and air inside a chamber. The water that is introduced into the chamber comes from the main system and as air is injected, surfactants will adhere to the wall of the air bubble to create a skin over it. The skin forms because the hydrophobic side of the surfactants will be attracted to the surface of the bubble by electrochemical forces. Eventually, the air bubbles injected inside the chamber will saturate with surfactants and will start overflowing inside a collecting cup.

The foam fractionator of the present invention provides for an improved filtration apparatus which utilizes a vortex inside a reaction chamber to achieve a skimming process. The foam fractionator involves the use of a motor, shaft, propellers, a plurality of reaction chambers, an air distributor and a collecting cup. A water pump is utilized to introduce water to the main reaction chamber and the motor can be located on the top of the unit so as to be attached to a shaft which turns the propellers.

The foam fractionator of the present invention comprises an outer casing adapted to receive water therein, the outer casing comprising a first opening for inserting a water inlet tube therethrough; an inner casing mounted within the outer casing, with the inner casing having a second opening for receiving the water inlet tube inserted through the first opening of the outer casing; a hollow member which extends through the inner casing, the hollow member comprising an air distributor at a bottom portion thereof and an air inlet

located at a top portion of the hollow member; a rotatable shaft which extends through the hollow member; a first propeller mounted on a lower end of the shaft and positioned at a bottom portion of the inner casing; and a second propeller mounted at the lower end of the shaft at a position below the first propeller, the second propeller being located below a lower end of the inner casing.

In the present invention, a rotation of the shaft causes a rotation of the first and second propellers, with the rotation of the first propeller drawing air into the hollow member through the air inlet such that the drawn-in air is led from the hollow member into at least the inner casing through the air distributor. The air led into the inner casing through the air distributor is mixed with water in the inner casing which is supplied to the inner casing through the water inlet to form an air/water mixture which rises inside the inner casing.

BRIEF DESCRIPTION OF THE DRAWINGS

A more complete appreciation of the invention and many of the attendant advantages thereof will be readily obtained as the same becomes better understood by reference to the following detailed description when considered in connection with the accompanying drawings, wherein:

FIG. **1** illustrates the foam fractionator of the present invention;

FIG. **2** illustrates the foam fractionator of FIG. **1** including a water flow therein;

FIG. **3** is a detailed view of a lower portion of the foam fractionator of the present invention; and

FIG. **4** is a view of a lower end of the foam fractionator of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to the drawings, wherein like reference numerals designate identical or corresponding parts throughout the several views, and more particularly to FIGS. **1** and **2** thereof, these figures illustrate the foam fractionator of the present invention. The foam fractionator constantly mixes water and air inside a chamber. FIGS. **1** and **2** illustrate an outer casing **1** and an inner casing **3** mounted within the outer casing **1**. The outer casing **1** includes a water inlet **5** which leads into the inner casing **3**. As illustrated in the figures, the outer casing **1** is adapted to receive water therein. Positioned within the inner casing **3** is a hollow member **7**. As illustrated in FIG. **1**, the hollow member **7** extends through a top opening of the outer casing **1** and through the inner casing **3**. At a lower end of the hollow member **7** an **10** air distributor **9** is positioned. The hollow member/air distributor arrangement (**7**, **9**) is mounted on a lower plate **11** which is positioned on the outer casing **1**. The outer casing **1** also includes an upper perforated plate **15** including perforations **15***a* and having an opening through which the hollow member **7** extends through.

The outer casing **1** can also include a cover **17** and an extended portion **17***a* which extends from the cover. A collection cup **19** can be positioned over the extended portion **17***a* of the outer casing **1**.

As illustrated in FIGS. **1** and **2**, the hollow member **7** extends beyond the top of the collection cup **19**. A rotatable shaft **21** extends longitudinally through the hollow member **7** and can be rotatably supported through for example bushings **23** within the hollow member **7**.

At the lower end of the rotatable shaft **21**, first and second propellers **25** and **27** are positioned. The first propeller **25** is an upper propeller and is positioned within the air distributor **9** at a lower end of the inner casing **3**. The second propeller **27** is a lower propeller and is positioned within a portion of the air distributor **9** that extends below the inner casing **3**. FIG. **3** shows an air inlet **27***a* to the lower propeller **27**.

A motor **29** or other type of moving mechanism can be positioned on the top portion of the rotatable shaft **21** by means of a chuck **31** as illustrated in FIGS. **1** and **2**. The motor **29** can be mounted to the outer casing **1** by means of a mounting mechanism **33** as illustrated in FIGS. **1** and **2**.

The foam fractionator of FIG. **1** further can include a water outlet **35** which can be located at a lower end of the outer casing and includes outlet pipes **35***a* and **35***b* as illustrated in FIG. **1**.

Positioned within the inner casing **3** are baffle plates or restrainers **37**. As illustrated in the drawings, the baffle plates **37** extend from an inner periphery of the inner casing **3** toward an outer periphery of the hollow member **7**. A space is maintained between an inner end of the baffle plates **37** and an outer surface of the hollow member **7** so as to permit water and air to pass therethrough. The baffle plates **37** can be inclined or have a cone shape as illustrated in the FIGS. **1** and **2** and can be positioned at intervals along a longitudinal direction of the hollow member **7** and inner casing **3** as illustrated in the drawings.

In the foam fractionator illustrated in FIGS. **1** and **2**, a first chamber **39** is defined within the hollow member **7**; a second chamber **41** is defined in the space defined by the inner casing **3**; a third chamber **43** is defined by the space between the inner casing **3** and the outer casing **1**; a fourth chamber **45** is defined by the top of the outer casing **1** and the upper perforated plate **15**; and a fifth chamber **47** is defined by the lower end of the outer casing **1** and the lower plate **11**.

As illustrated in FIGS. **1** and **2**, the water outlet **35** can be positioned within the lower chamber **47**. Also, the lower plate **11** can include a fifth chamber inlet **49** or perforations **49***a* (see FIGS. **3** and **4**) for communicating the third chamber **43** and the fifth chamber **47**.

Operation of the present invention will now be described with reference to FIG. **2**. To start operation, the motor **29** is activated so as to turn the shaft **21** and thereby rotate the upper and lower propellers **25** and **27**. Once the propellers **25** and **27** are rotating, the upper propeller **25** will create a vortex **100** that will suck air from the atmosphere into the first chamber **39** defined by the hollow member **7**. As contact is made between the upper propeller **25** and the incoming air, the incoming air will be broken and dispersed by the air distributor **9**. Due to the action of the upper propeller **25**, water which is introduced into the outer casing **3** by way of the water inlet **5** and is already inside the inner casing **3**, will mix with the air. Therefore, water from the system to be filtered will enter through the water inlet **5** directly into the inner casing **3** where it is received by the vortex action created by the upper propeller **25**. As water mixes with air, it starts to rise inside the secondary chamber **41** and will attract matter in the water. It is noted that the movement of the air and water is illustrated by arrows in FIG. **2** (such as, for example, in the form of a foam vortex **200**).

Once the air/water mixture leaves the secondary chamber **41**, the air will pass to the fourth chamber **45** with accumulated matter and the water will go down due to the action of gravity as further illustrated by the arrows in FIG. **2**. The lower propellers **27** create a counter-current effect which will be achieved by a second vortex. As described above, the

lower propeller **27** is attached to the lower end of the shaft **21** within a portion of the air distributor **9** which extends below the inner casing **3**. The lower propeller **27** creates an action which is simultaneous but separate from the action created by the upper propeller **25**. That is, the upper propeller **25** aerates the second chamber **41**, while the lower propeller **27** aerates the third chamber **43**. Air reaches the second propeller **27** by drawing air from the distributor through a bushing located at the bottom of the inner casing **3** or through specially located perforations **27***a*. This operation makes the unit twice as effective because it permits the water to be skimmed twice before returning to the main system, to prevent any re-incorporation of unskimmed matter, during a first fractionating stage, into the returning water flow.

To further improve the contact time between the air and water, as noted above, the inner casing **3** includes the baffles or restrainers **37**. The restrainers are positioned on an inner periphery of the inner casing **3** and extend to but do not touch an outer periphery of the hollow member **7**. The space between the inner end of the baffle plates and the outer periphery of the hollow member **7** enables the air/water mixture to rise at a slow rate within the inner casing **3**. The swirling effect created by the upper propeller **25** will be promulgated by these restrainers, to increase the contact between the incoming water and the drawn-in air. Since the action inside the secondary chamber **41** is not a counter-current action, incorporation of several restrainers **37** as illustrated in FIGS. **1** and **2** will help achieve the desired restraining effect.

Therefore, once the rising air/water mixture reaches the top of the inner casing **3**, a portion of the air/water mixture rising into the fourth chamber **45** will cause a foam created by the air/water mixture to rise and be finally collected in the collection cup **19**.

With regard to the propellers **25** and **27**, as illustrated in FIGS. **3** and **4**, the propellers **25** and **27** can be blade turbine type propellers having straight vanes that can form a 90-degree angle with the lower end of the casing. The blades are designed to operate at very high speeds and are designed to draw air from the top as explained above and properly mix the air with the incoming liquid. The blades are also designed to displace the air sideways away from the center of the first chamber so as to increase the contact time of the water/air mixture. The blades are also designed to minimize any axial flow patterns so as to help achieve the desired sideways flow of air which is drawn in from the top.

The combination of the propellers **25**, **27**, restraining devices **37** and chambers **39**, **41**, **43**, **45** and **47** of the present invention create a proper air/water mixture to achieve the desired filtering of water in the system. That is, the apparatus of the present invention creates the proper air/water bubble size in the air/water mixture which is important for waste water treatment. Applicant notes that if the air bubble size is too small, the air bubble will not be able to float enough to reach the collecting cup **19**. If, on the contrary, the air bubbles are too large, they rise to the surface too fast and the surfactants will not have enough time to stick to the bubble surface. Applicant further notes that a recommended bubble average size is about 0.8 mm to maximize the performance of the unit of the present invention.

The present invention also provides for a desired air-water relation. That is, there must be a proper relation between the amount of water entering the chamber and the amount of air injected. If too much air is injected, then the foam collected inside the cup **19** will be excessively wet. If too little air is injected, then the skimming process will be extremely slow and ineffective.

Additionally, the present invention achieves a desired contact time between the air bubbles and the water. Presuming that the air bubble size and air/water relation are satisfactory, then the contact time should be lengthened as much as possible. In this way, the air bubbles will be covered with surfactants until saturation.

The apparatus of the present invention as described above including the restrainers and propellers achieves the desired air bubble size, air/water relation and contact time for permitting an efficient filtering of a water system.

The apparatus of the present invention is capable of preventing the introduction of fine air bubbles since it is important to prevent these fine air bubbles from entering into the main system. This is particularly important in systems that house marine invertebrates, specifically corals, since air bubbles can, and will, lodge in their tissue. If this air is not removed, the animal's tissue will slowly recede to expose the skeleton until it dies. As air is broken by the propeller inside the unit, the size of some bubbles may be too small so as not to create a strong buoyancy. This may enable outcoming water to carry them right out of the unit. The utilization of the lower plate **11** and fifth chamber **47** of the present invention creates a longer path of resistance to the bubbles that wears the outcoming water's momentum so as to reduce any air leakage to the main system.

With regard to the fifth chamber **47**, as noted above, this chamber is useful in preventing water to quickly flow back into the system. The fifth chamber **47** creates a path of resistance to bubbles which are too small to rise within the inner casing **3**. The length of the fifth chamber **47** is based on design considerations and can be longer than that illustrated in the drawings. The lower plate **11** can include a number of perforations **49***a* and the fifth chamber **47** can have a length which is long enough to prevent fine air bubbles with weak buoyancies to enter the main system. Therefore, the air bubble concentration would be higher in the upper part of the fifth chamber **47**. Thus, the fifth chamber **47** acts as a resistance path that will decrease the water's velocity around the area of highest air concentration to allow the bubbles to rise more easily. It is noted that the effectiveness of the fifth chamber **47** can also be increased by filling it with inner sponge material so as to trap any fine bubbles which enter the fifth chamber.

Thus, the present invention provides for a foam fractionator which creates a vortex and works as a protein skimmer which is designed to work with, for example, salt water aquarium systems. The apparatus of the present invention can produce a great number of appropriately sized air bubbles with an equally appropriate surface area. Organic materials that dissolve in water as noted above can have hydrophilic (water attracting) and hydrophobic (water repelling) features. The foam fractionator of the present invention mixes water with air inside a chamber such that the water introduced into the chamber that comes from the main system and air which is injected into the main system will cause formation of bubbles such that the surfactants will adhere to the bubbles. These air bubbles which will upwardly flow within the system will saturate with the surfactants and overflow inside a collecting cup.

Obviously, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that, within the scope of the appended claims, the invention may be practiced otherwise than as specifically described herein.

What is claimed as new and desired to be secured by Letters Patent of the United States is:

1. A foam fractionator comprising:

an outer tubular casing adapted to receive water therein, said outer casing comprising a first opening for inserting a water inlet tube therethrough;

an inner tubular casing mounted within said outer casing, said inner casing having a second opening for receiving the water inlet tube inserted through said first opening of the outer casing, said inner tubular casing being smaller than said outer tubular casing so as to define a space there between;

a hollow tubular member which extends through said inner casing, said hollow member comprising an air distributor at a bottom portion thereof, and an air inlet is located at a top portion of said hollow member;

a rotatable shaft which extends through said hollow member;

a first propeller mounted on a lower end of the shaft and positioned at a bottom portion of said inner casing; and

a second propeller mounted at the lower end of the shaft at a position below said first propeller, said second propeller being located below a lower end of said inner casing;

means for receiving foam mounted at a vicinity of a top portion of the outer casing;

wherein a rotation of said shaft causes a rotation of said first and second propellers, said rotation of the first propeller drawing air into said hollow member through said air inlet such that the drawn-in air is led from said hollow member into at least said inner casing through said air distributor, the air led into said inner casing through said air distributor being mixed with water in said inner casing which is supplied to said inner casing through said water inlet to form an air/water mixture which rises inside the inner casing.

2. A fractionator according to claim 1, further comprising:

an upper perforated plate positioned in said outer casing above said inner casing, wherein the air/water mixture rising in said inner casing passes through said upper perforated plate and is collected in a collection cup which is mounted at a vicinity of a top portion of the outer casing.

3. A fractionator according to claim 1, wherein said inner casing comprises a plurality of baffle plates which extend from an inner wall of the inner casing toward the hollow member, wherein a space is maintained between an inner end of said baffle plates and an outer surface of said hollow member, said baffle plates being mounted at intervals along a longitudinal direction of said hollow member so as to lower a rising rate of the air/water mixture.

4. A fractionator according to claim 1, wherein the first and second propellers are positioned within the air distributor of the hollow member.

5. A fractionator according to claim 4, wherein a lower end of said air distributor extends through a bottom portion of said inner casing and said air distributor is mounted on a lower plate mounted on said outer casing.

6. A fractionator according to claim 5, wherein said lower plate is a perforated plate.

7. A fractionator according to claim 5, wherein the lower plate comprises an opening.

8. A fractionator according to claim 5, wherein a lower chamber is defined between the lower plate and a bottom end of the outer casing, the lower chamber comprising a water outlet tube.

9. A fractionator according to claim 1, wherein an upper perforated plate and a top end of the outer casing define an upper chamber which receives the air/water mixture, wherein water which does not pass through said upper perforated plate is drawn downward within said space defined between said inner casing and said outer casing by gravity.

10. A fractionator according to claim 4, wherein said lower propeller draws air into a space defined between said outer casing and said inner casing.

11. A fractionator according to claim 1, wherein a motor is operatively connected to said rotatable shaft for rotating said shaft.

* * * * *

US006743218B2

(12) **United States Patent**
Maginot et al.

(10) **Patent No.: US 6,743,218 B2**
(45) **Date of Patent: Jun. 1, 2004**

(54) **RETRACTABLE CATHETER SYSTEMS AND ASSOCIATED METHODS**

(75) Inventors: **Paul J. Maginot**, Fishers, IN (US); **Thomas J. Maginot**, Crown Point, IN (US)

(73) Assignee: **CathLogic, Inc.**, Crown Point, IN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 294 days.

(21) Appl. No.: **10/006,799**

(22) Filed: **Dec. 4, 2001**

(65) **Prior Publication Data**

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Related U.S. Application Data

(63) Continuation-in-part of application No. 09/716,815, filed on Nov. 20, 2000, and a continuation-in-part of application No. 09/716,308, filed on Nov. 20, 2000, now Pat. No. 6,585,705, said application No. 09/716,815, is a continuation-in-part of application No. 09/443,876, filed on Nov. 19, 1999, now Pat. No. 6,475,207, said application No. 09/716,308, is a continuation-in-part of application No. 09/246,831, filed on Feb. 8, 1999, now Pat. No. 6,190,371.

(60) Provisional application No. 60/116,017, filed on Jan. 15, 1999.

(51) **Int. Cl.**[7] **A61M 31/00**

(52) **U.S. Cl.** **604/510**; 604/508; 604/523; 604/6.16; 604/28; 604/29; 604/165.02

(58) **Field of Search** 604/4.01, 6.16, 604/19, 27–29, 43, 500, 506–508, 510, 93.01, 158, 163, 164.01, 164.02, 164.04, 164.08, 164.09, 165.01, 165.02, 167.01, 167.04, 174, 263, 264, 523, 533, 540–544

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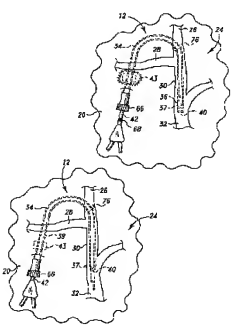
Primary Examiner—Brian L. Casler
Assistant Examiner—Jennifer Maynard
(74) *Attorney, Agent, or Firm*—Paul J. Maginot

(57) **ABSTRACT**

A method of performing dialysis with a catheter system which includes (i) a working catheter having a distal working orifice, and (ii) a guide catheter having a guide lumen and a distal guide orifice is disclosed. The method includes the step of locking the working catheter in an operative position in which (i) the working catheter extends through the guide lumen of the guide catheter and out of the distal guide orifice of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned outside of the guide catheter. The method further includes the step of performing a dialysis procedure including advancing and withdrawing blood through the working catheter while the working catheter is locked in the operative position. Moreover, the method includes the step of, after the dialysis procedure performing step, locking the working catheter in a stowed position in which (i) the working catheter extends into the guide lumen of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned within the guide lumen of the guide catheter.

67 Claims, 44 Drawing Sheets



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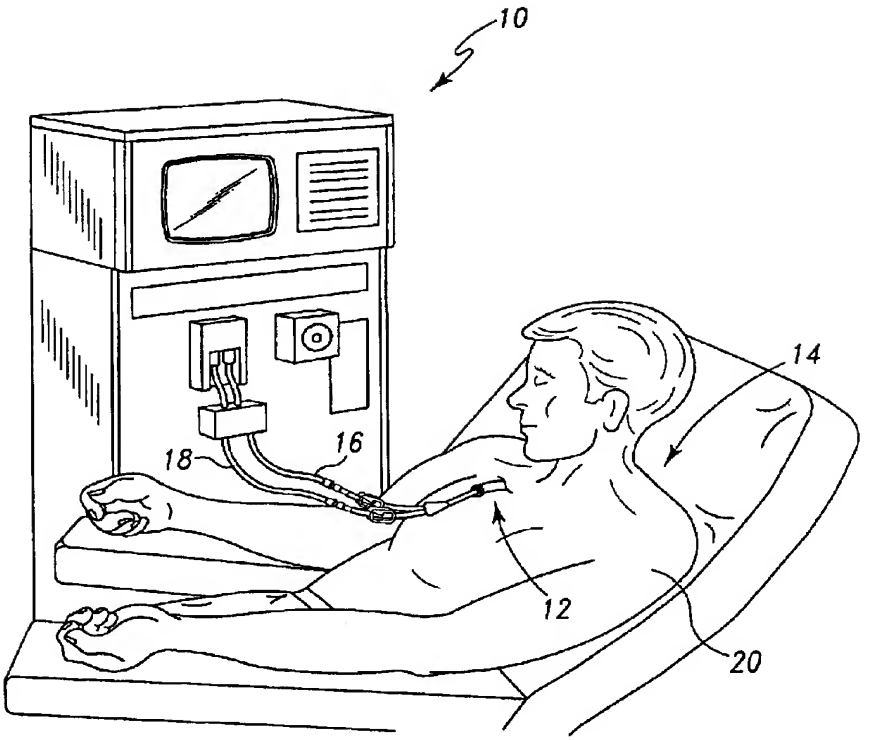


Fig. 1

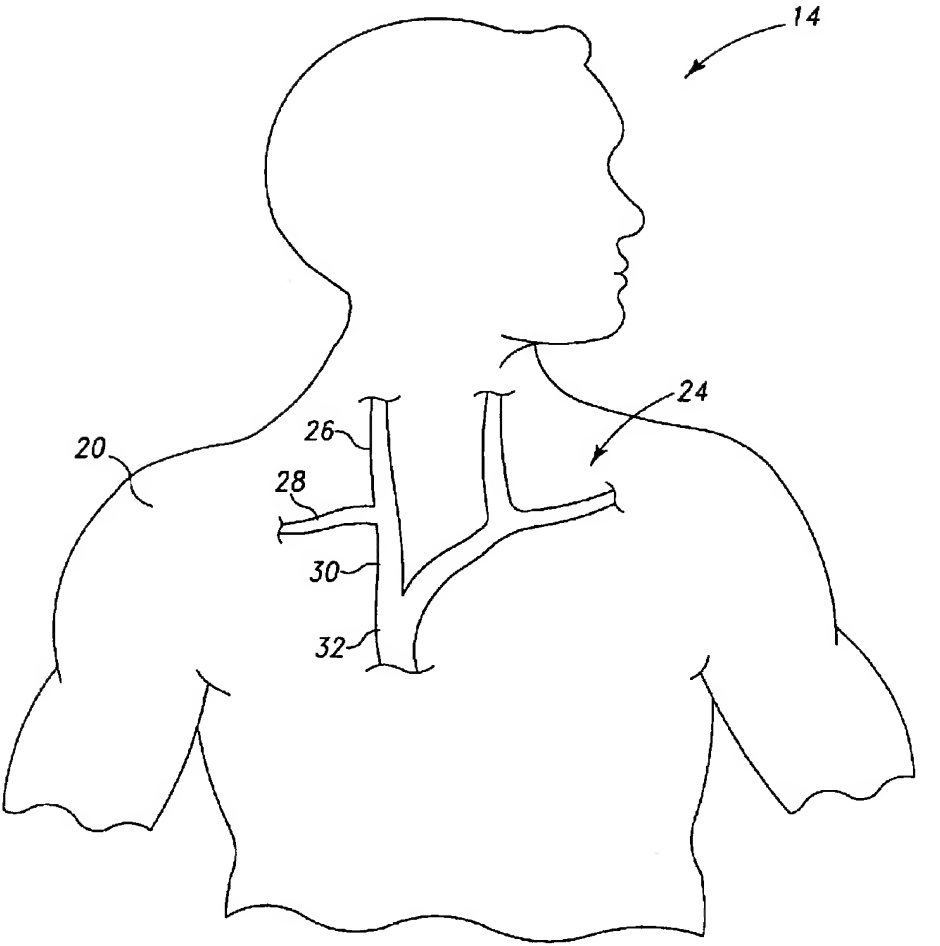
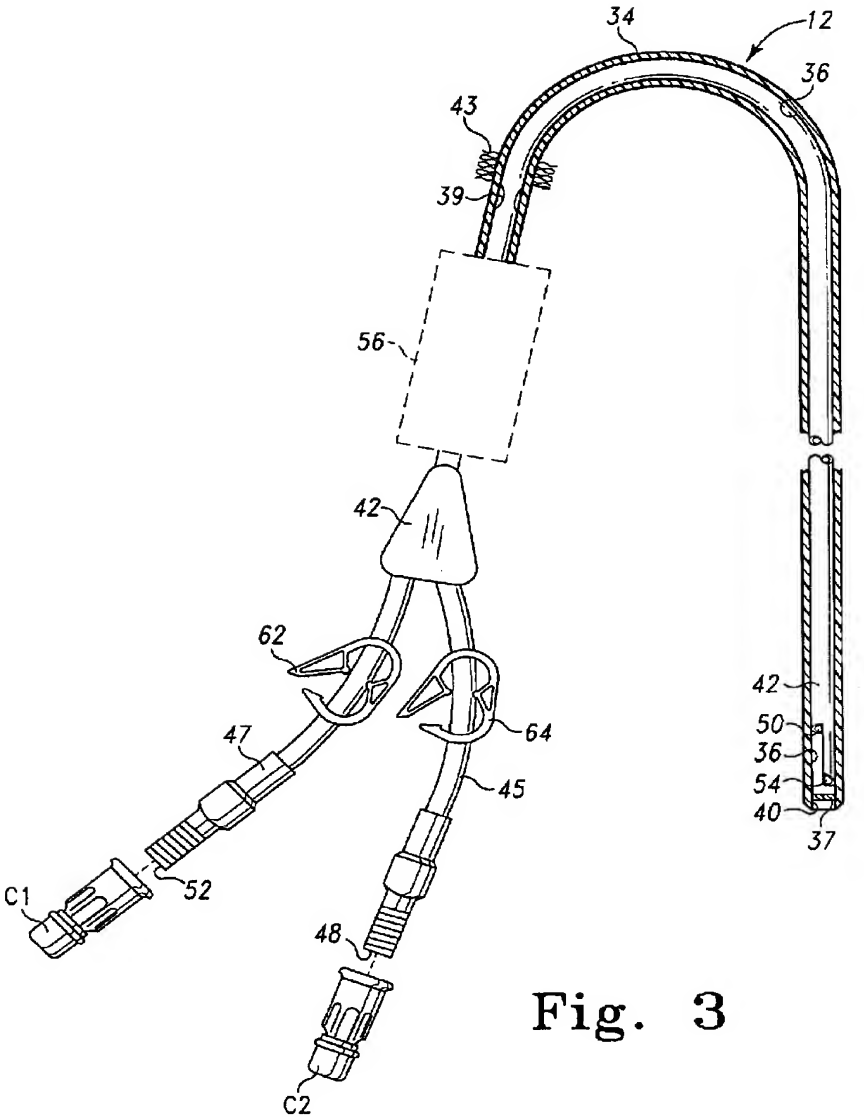


Fig. 2



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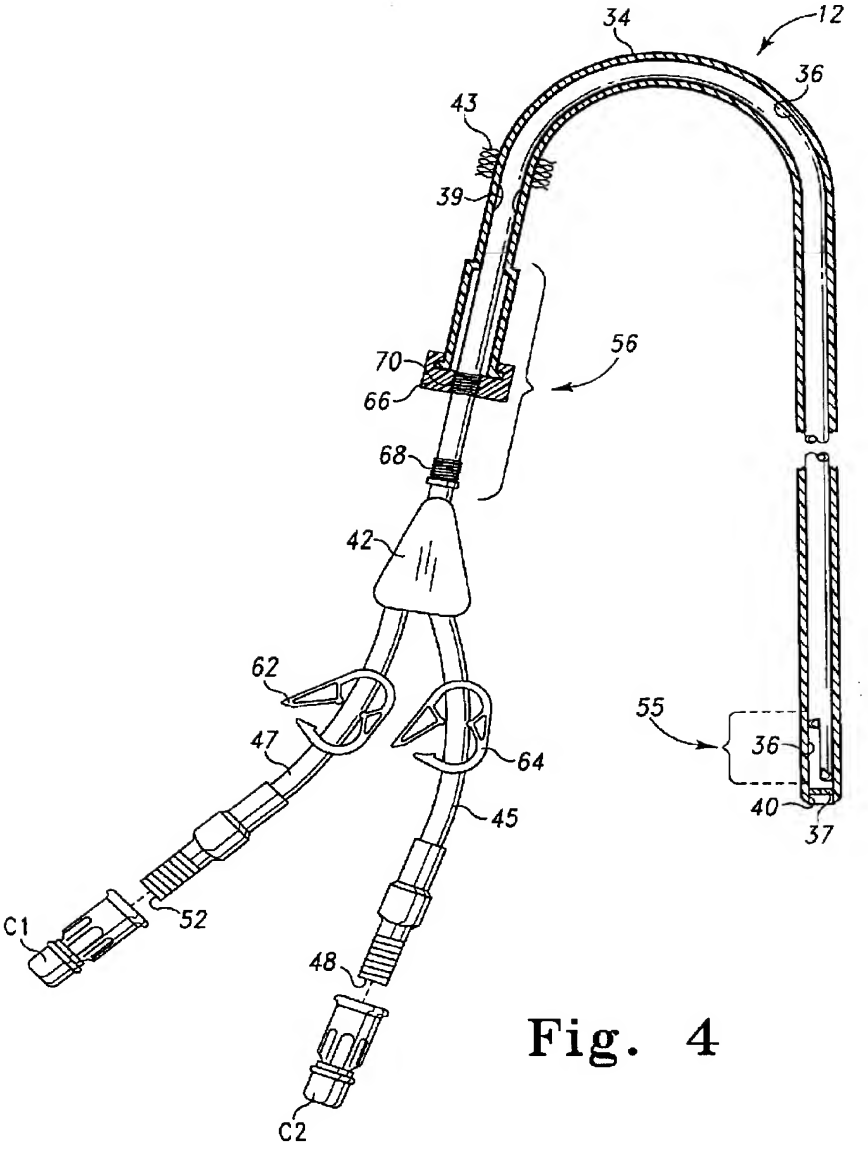


Fig. 4

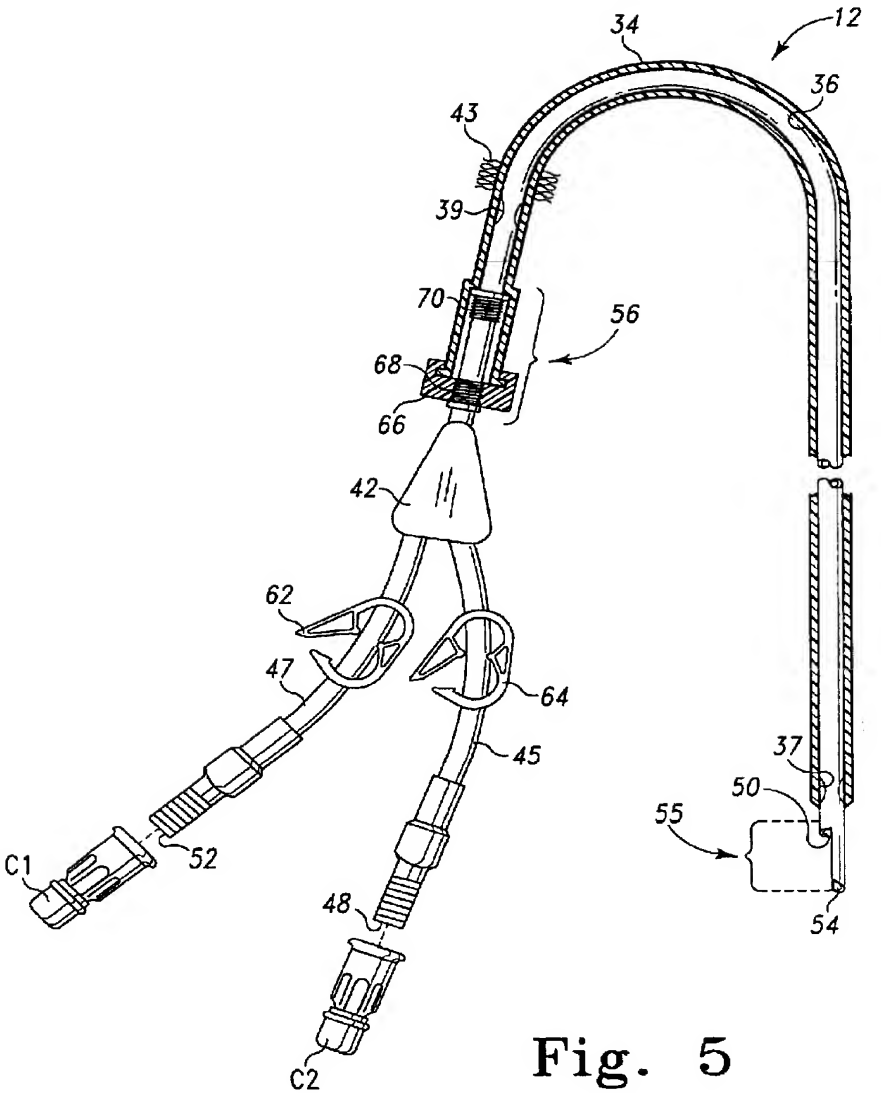


Fig. 5

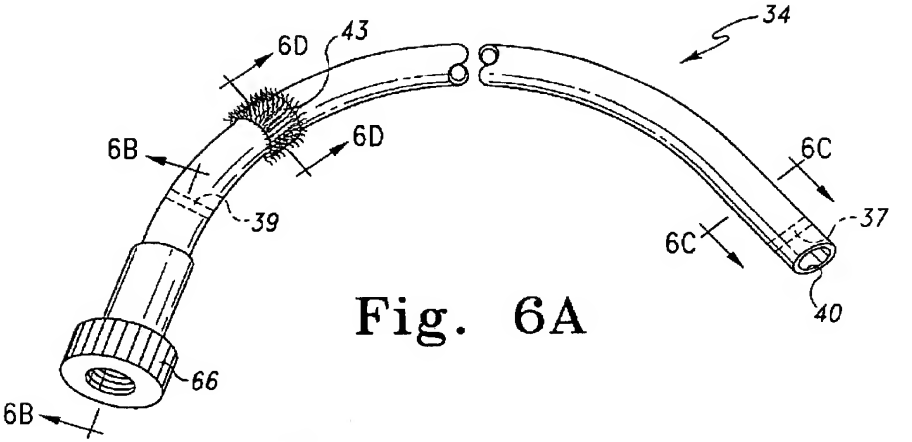


Fig. 6A

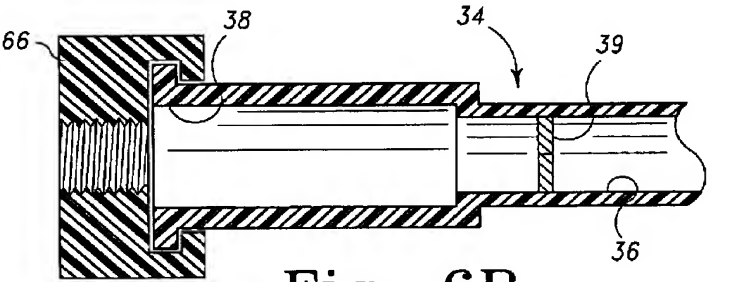


Fig. 6B

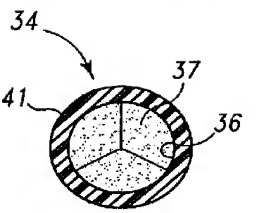


Fig. 6C

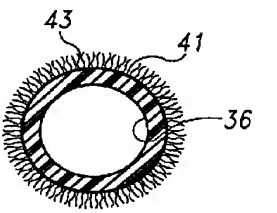


Fig. 6D

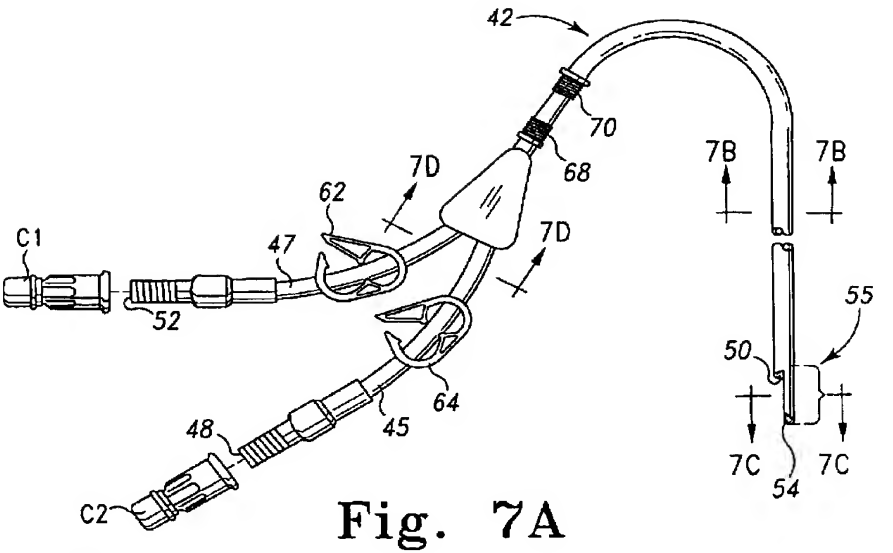


Fig. 7A

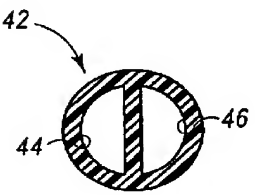


Fig. 7B

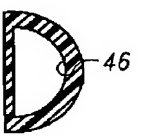


Fig. 7C

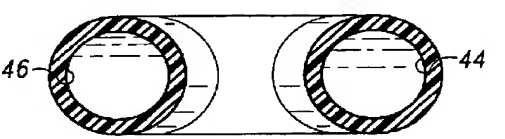


Fig. 7D

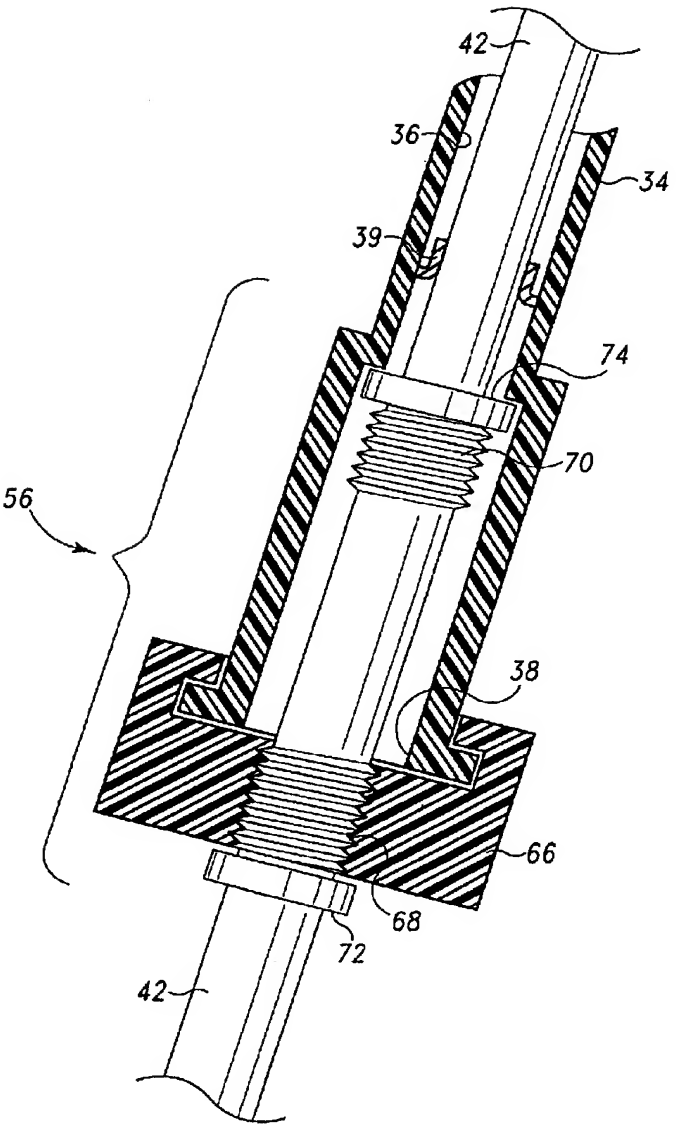


Fig. 8

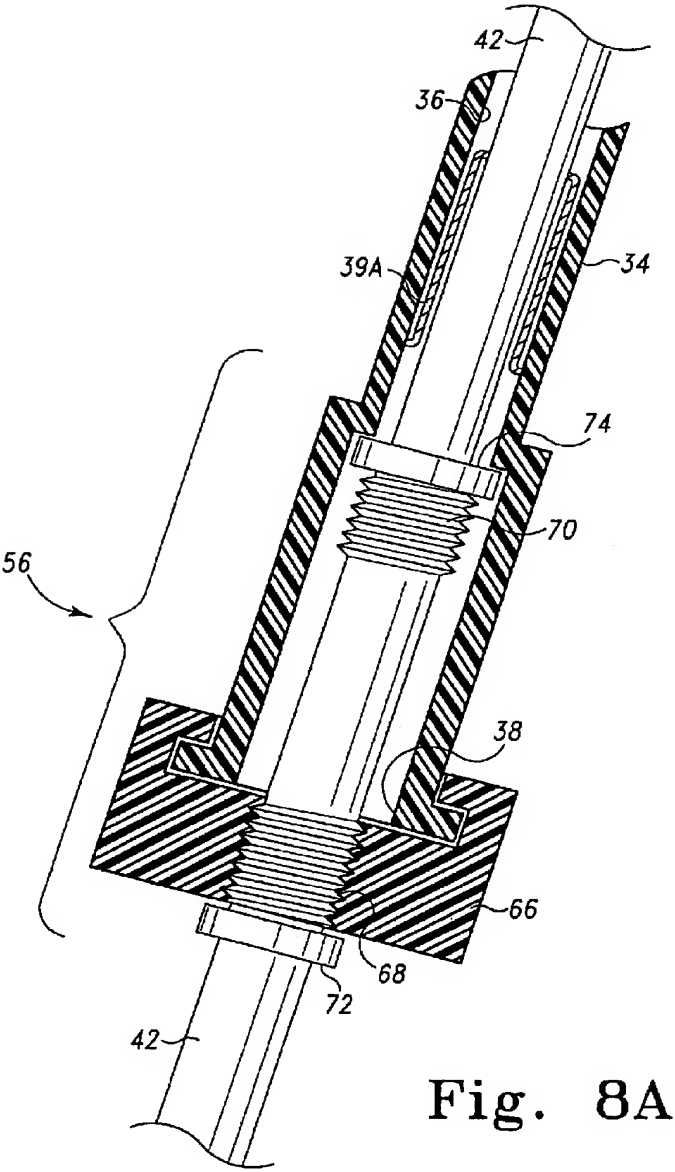


Fig. 8A

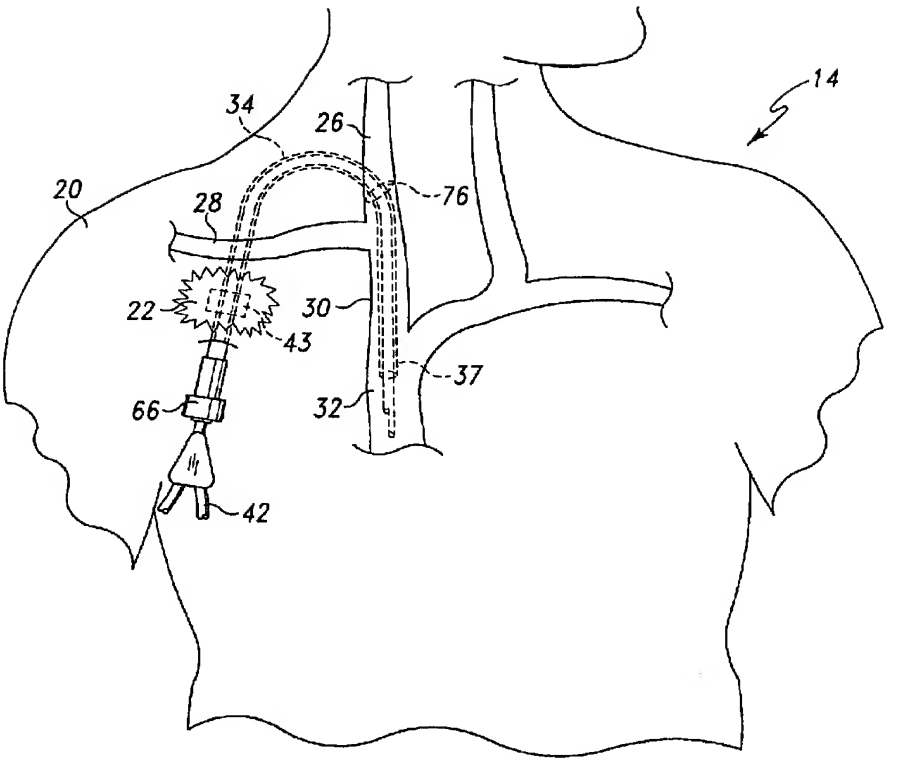
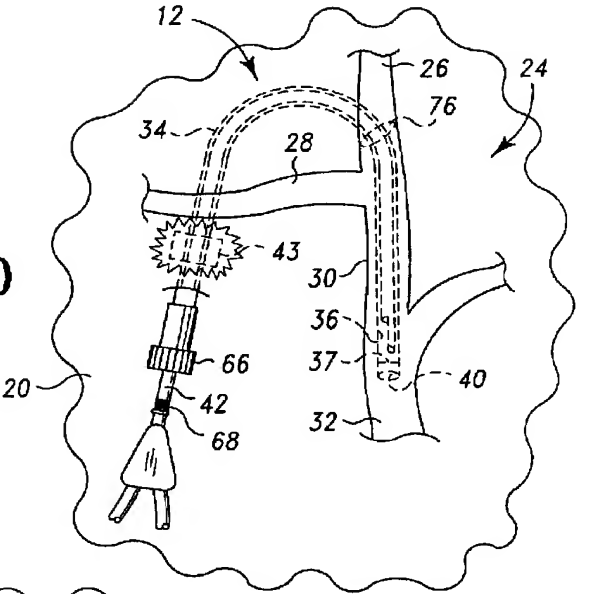


Fig. 9

Fig. 10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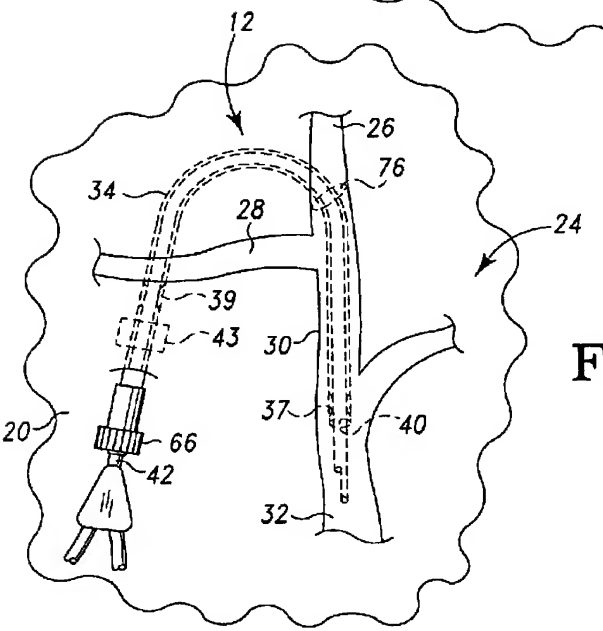
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Fig. 11

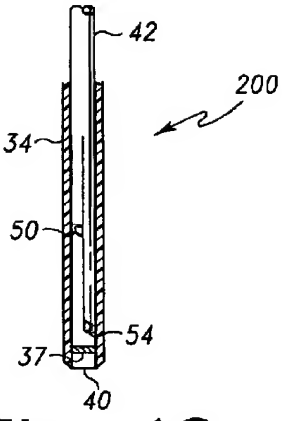

Fig. 13

Fig. 12

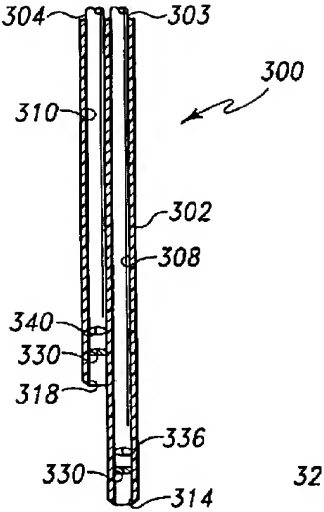
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Fig. 15

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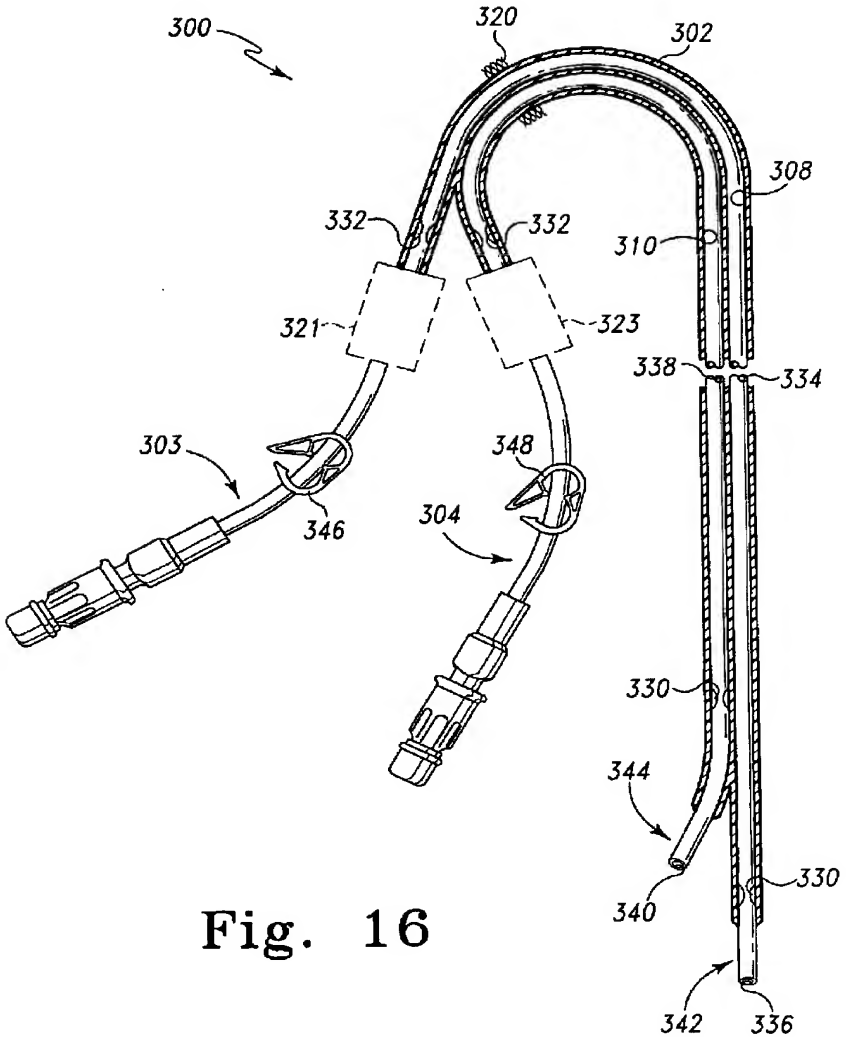
Fig. 14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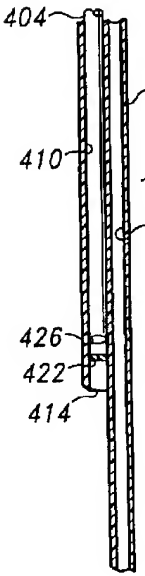
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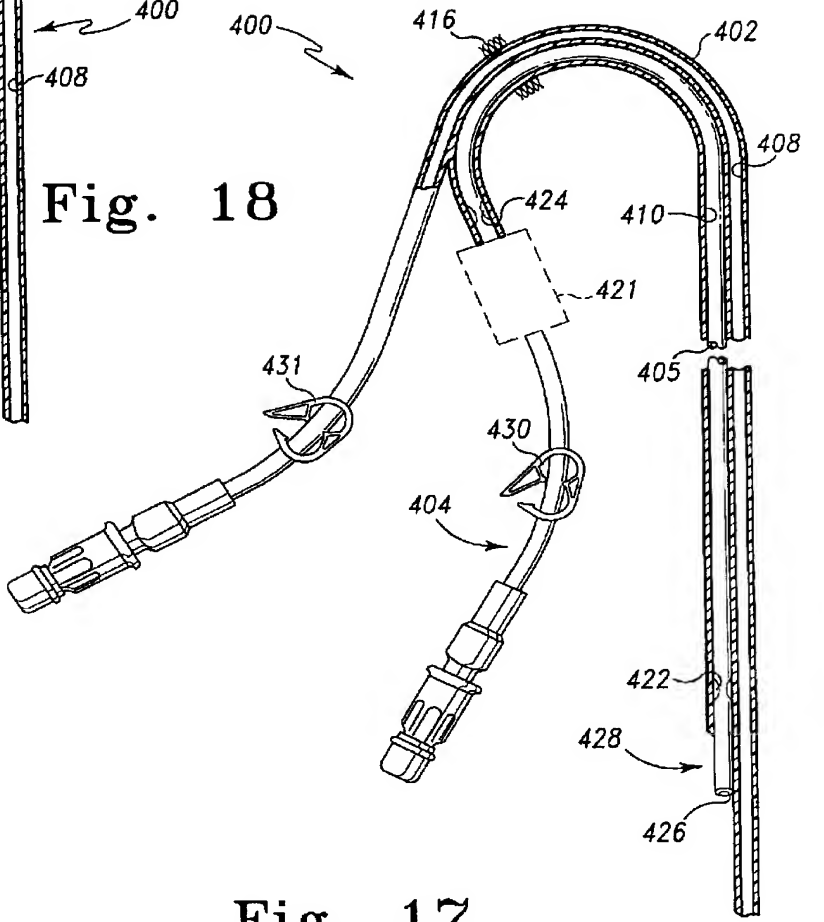
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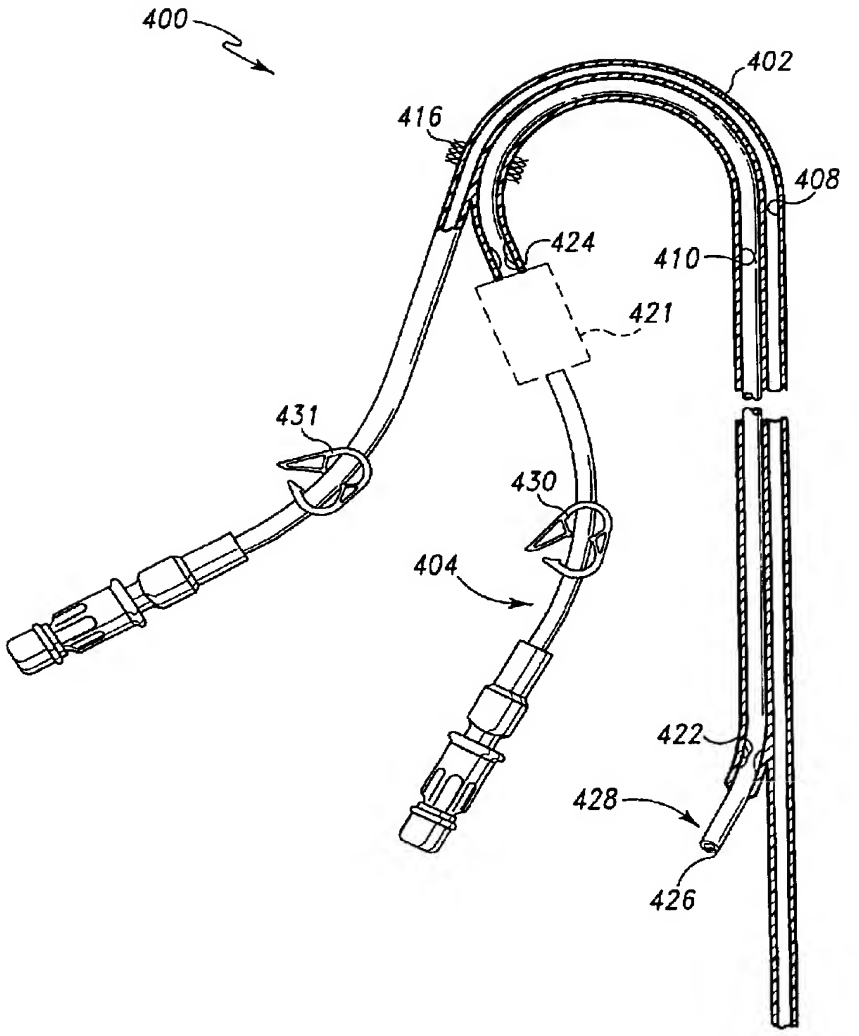

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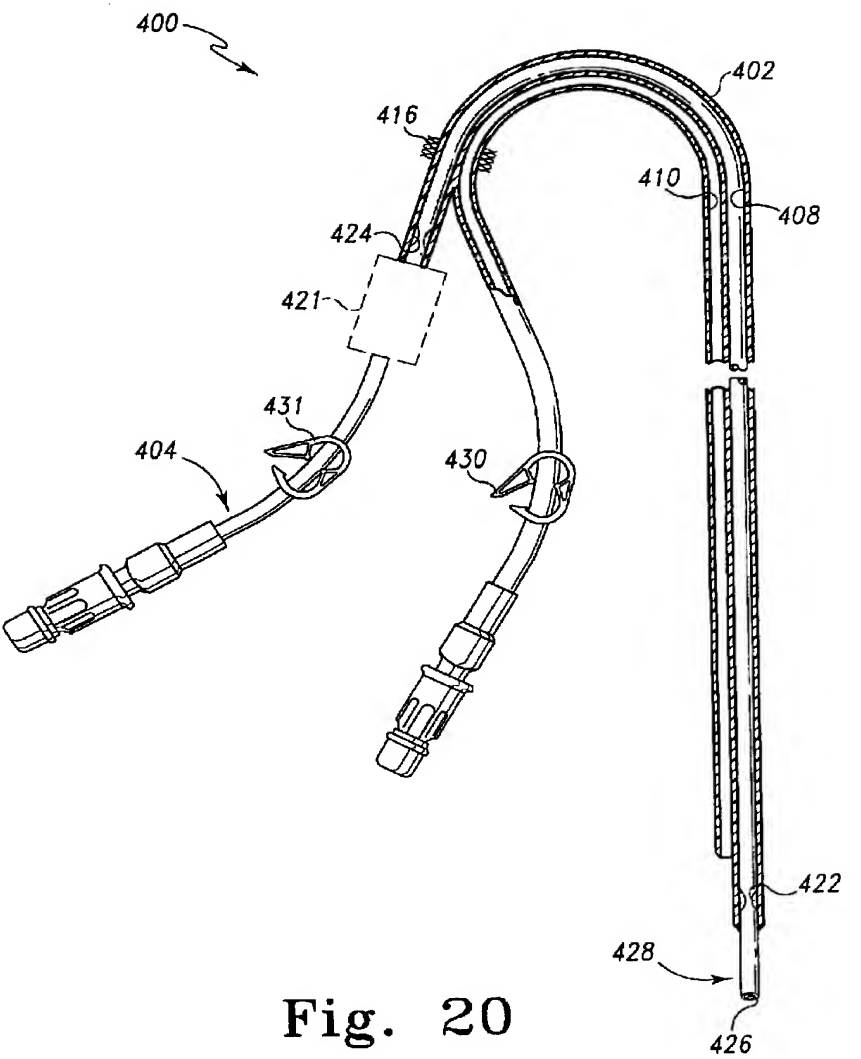

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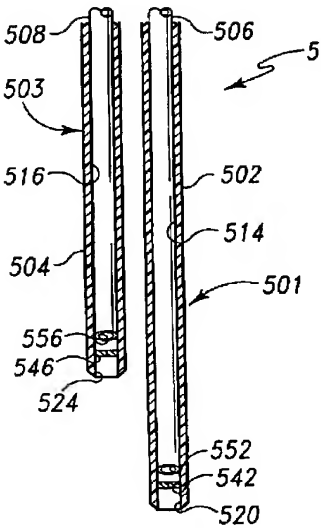
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Fig. 22

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Fig. 21

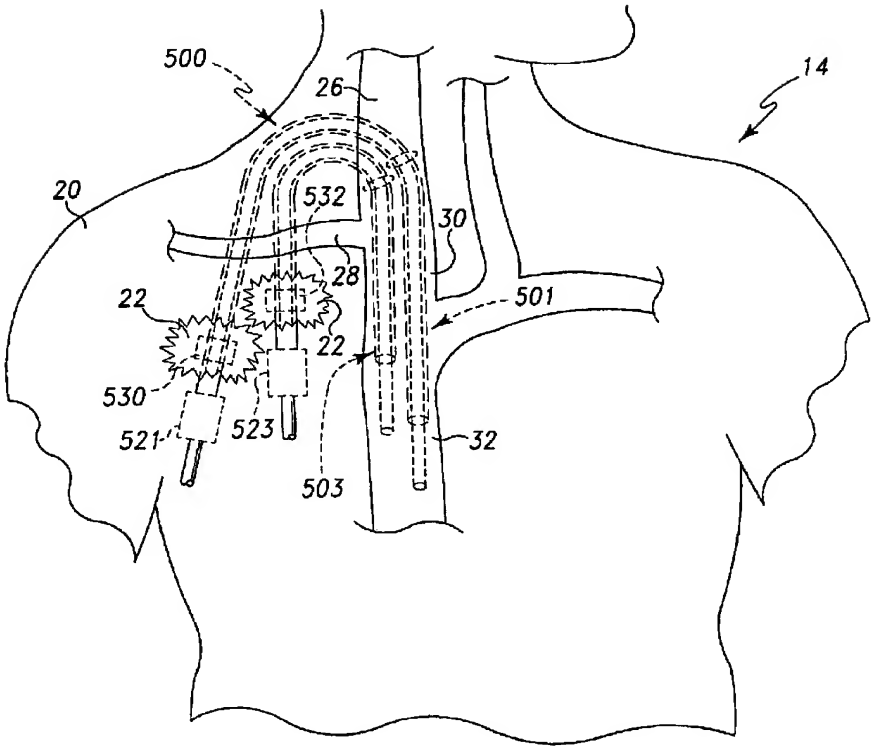

Fig. 23

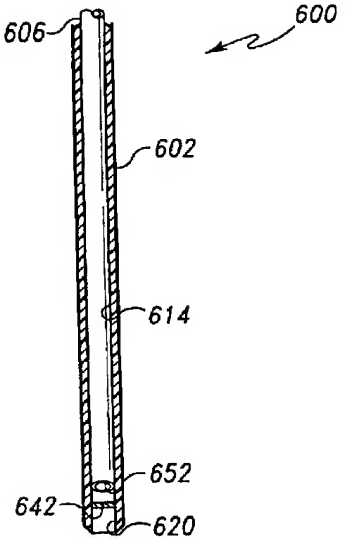
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Fig. 25

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Fig. 24

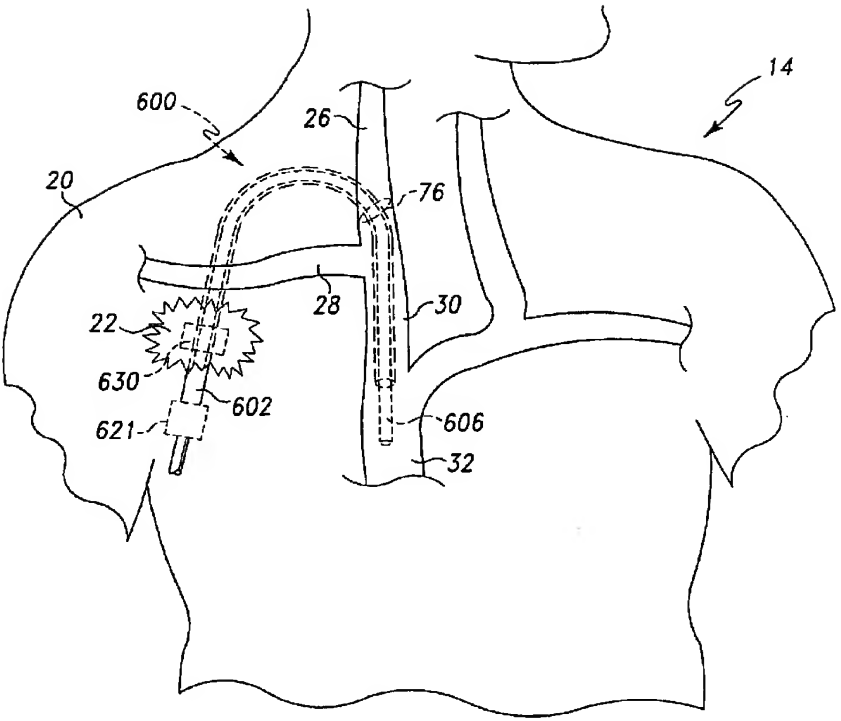

Fig. 26

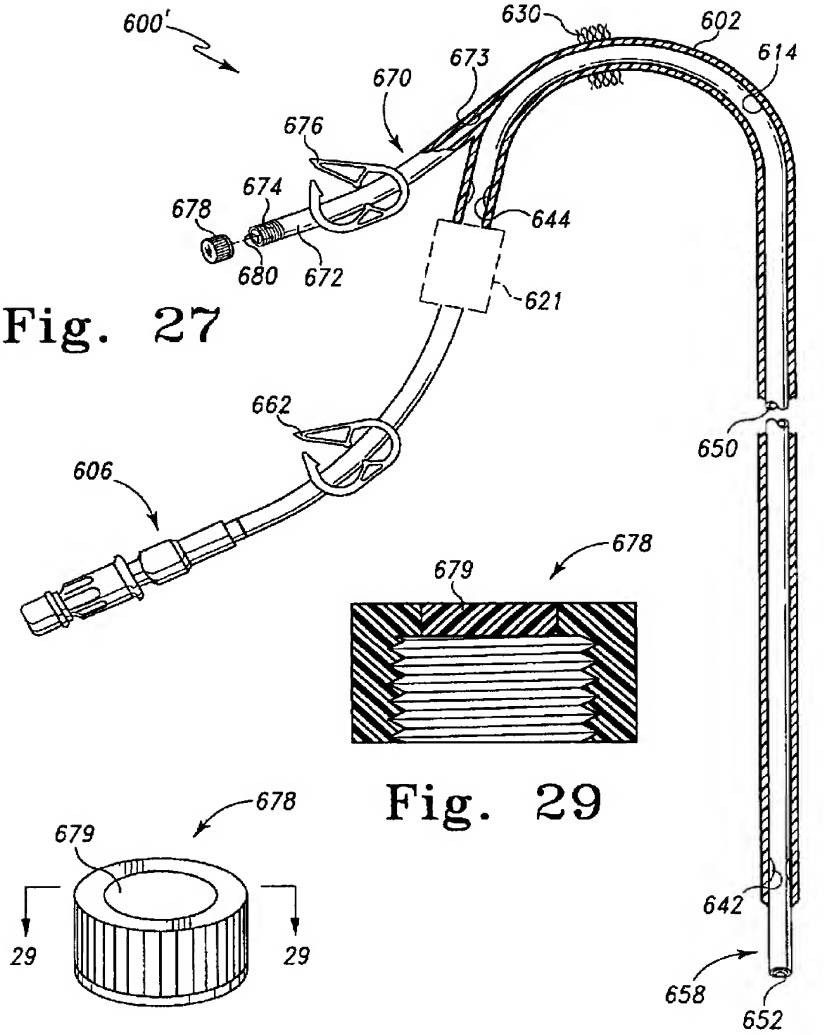

Fig. 27

Fig. 29

Fig. 28

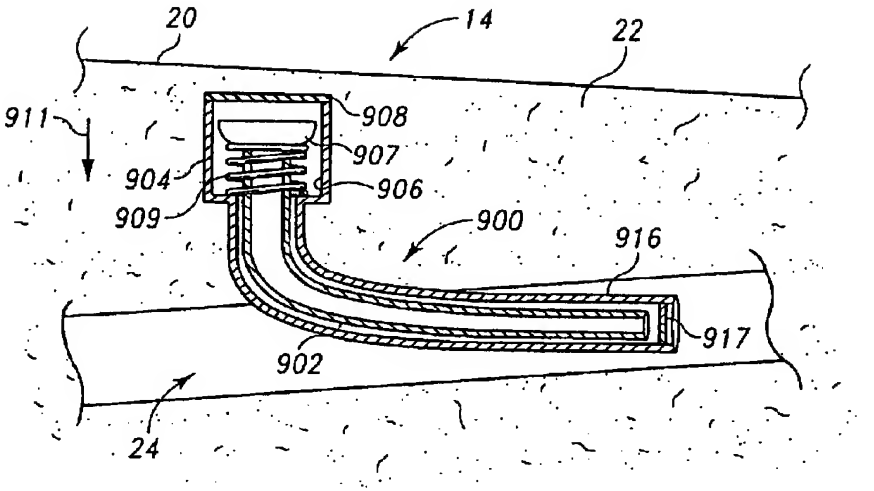

Fig. 30

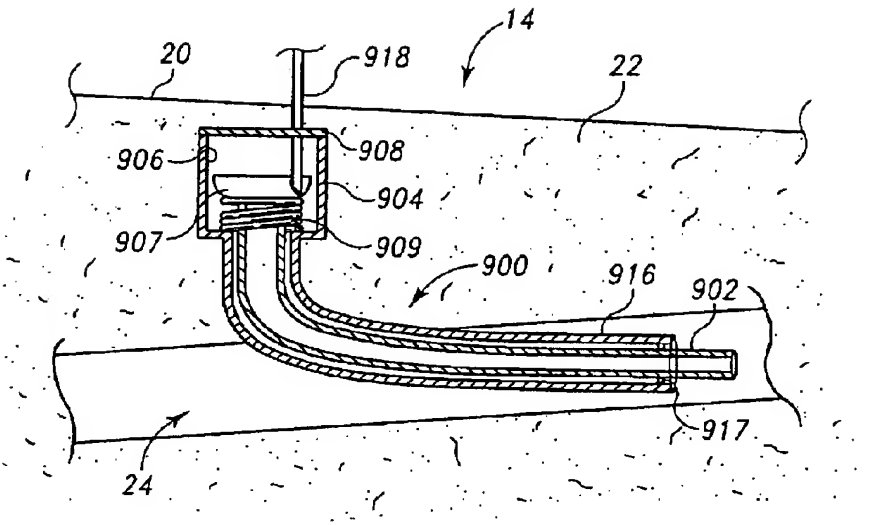

Fig. 31

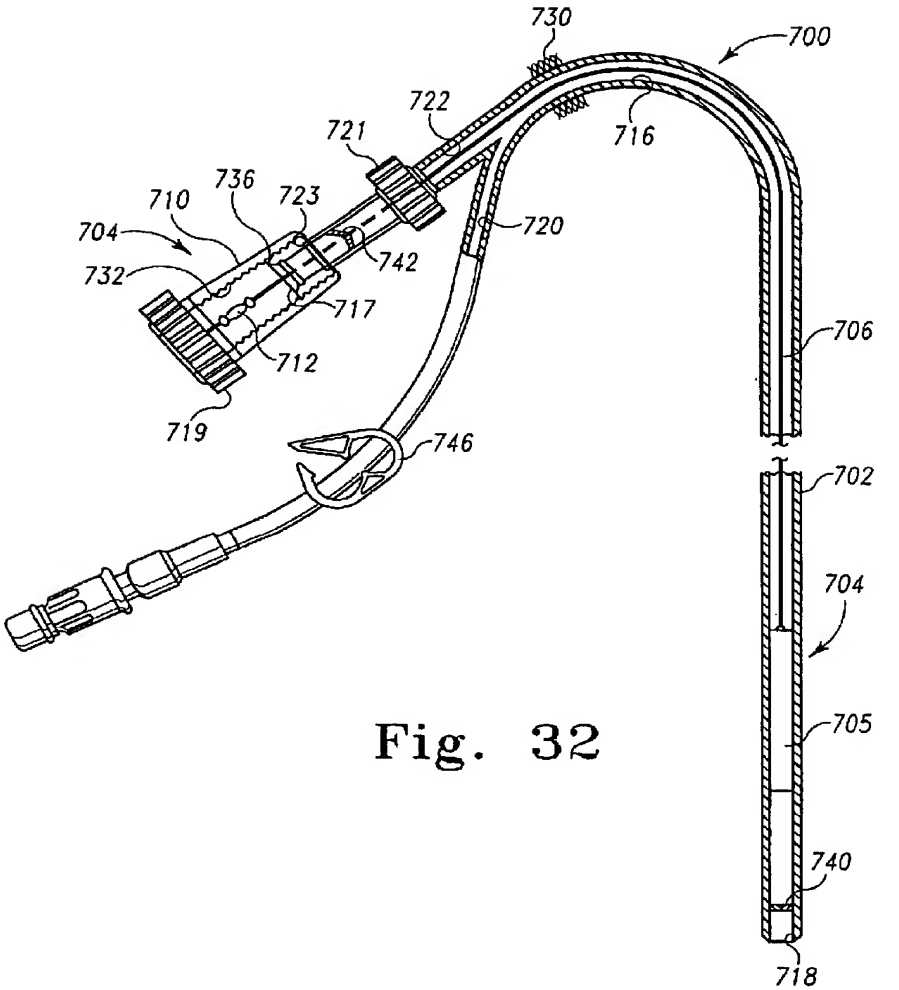
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Fig. 32

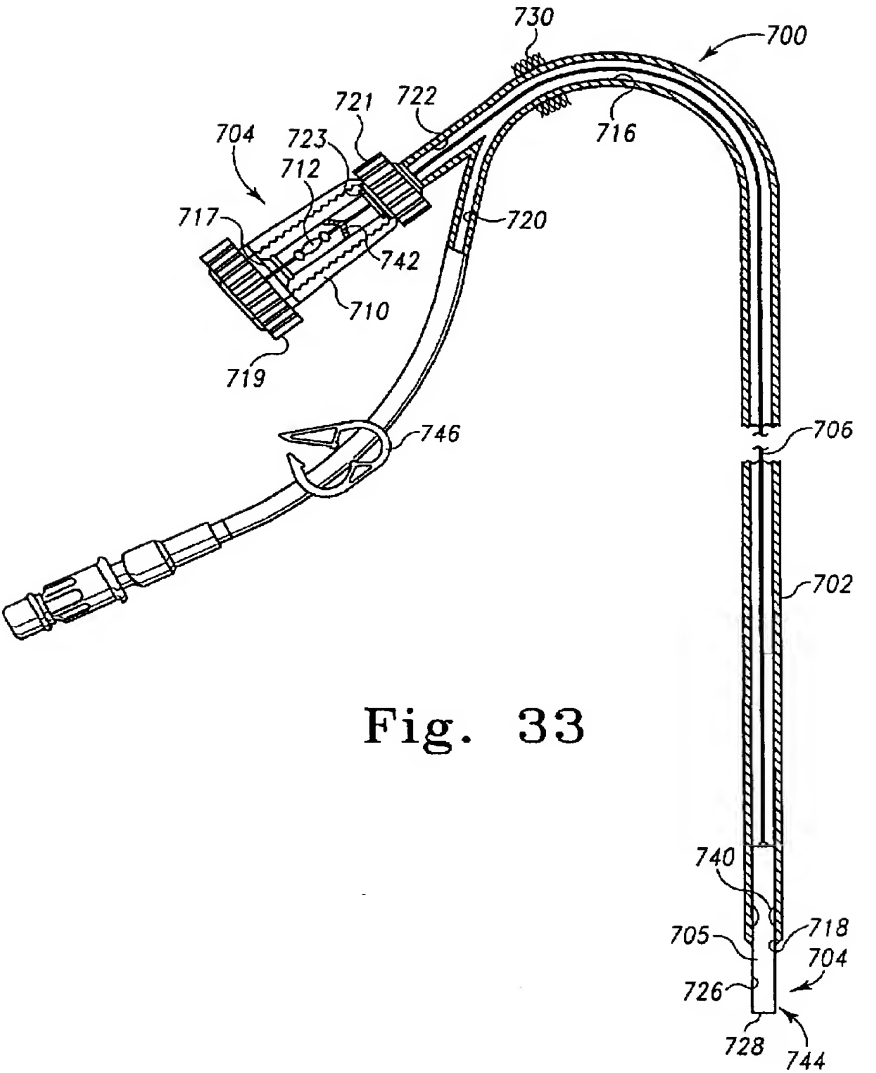
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Fig. 33

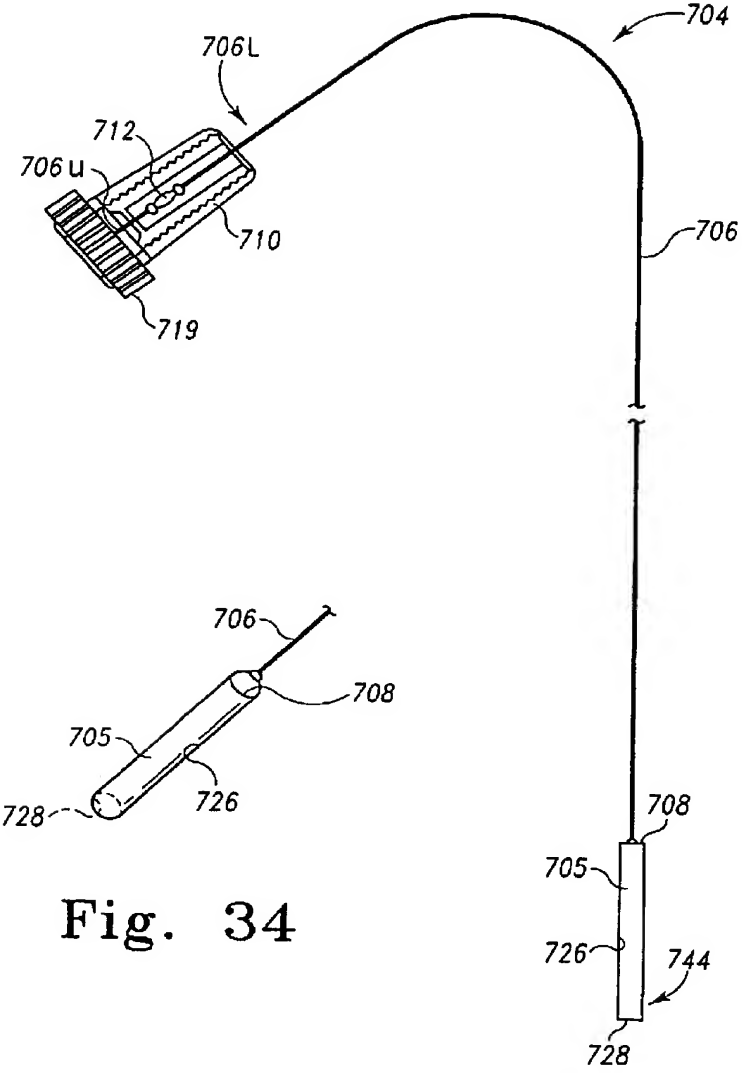
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Fig. 34

Fig. 35

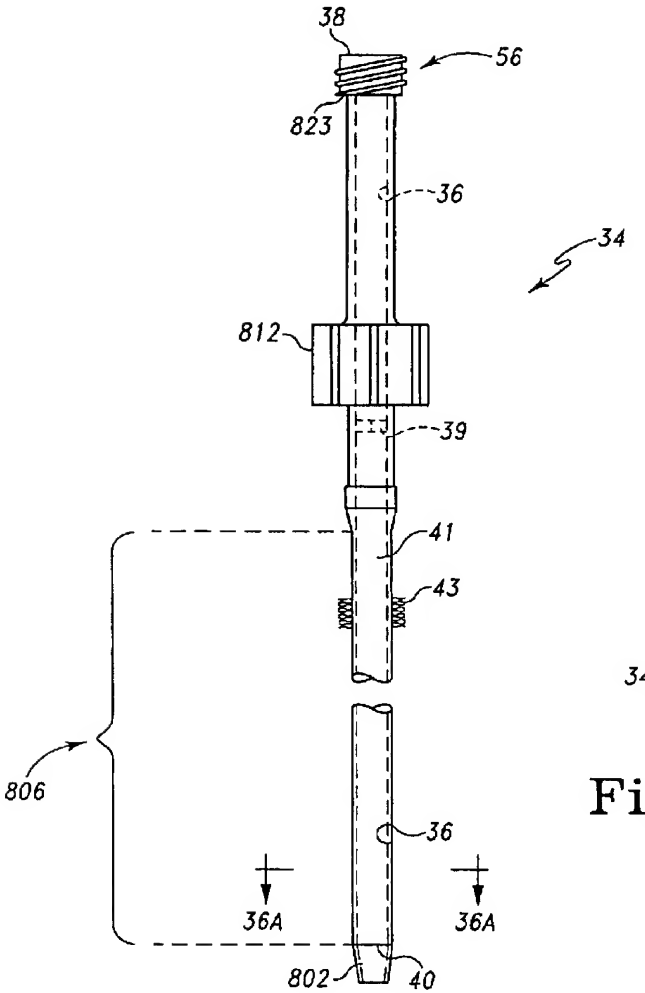

Fig. 36

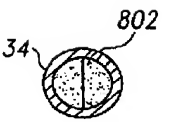

Fig. 36A

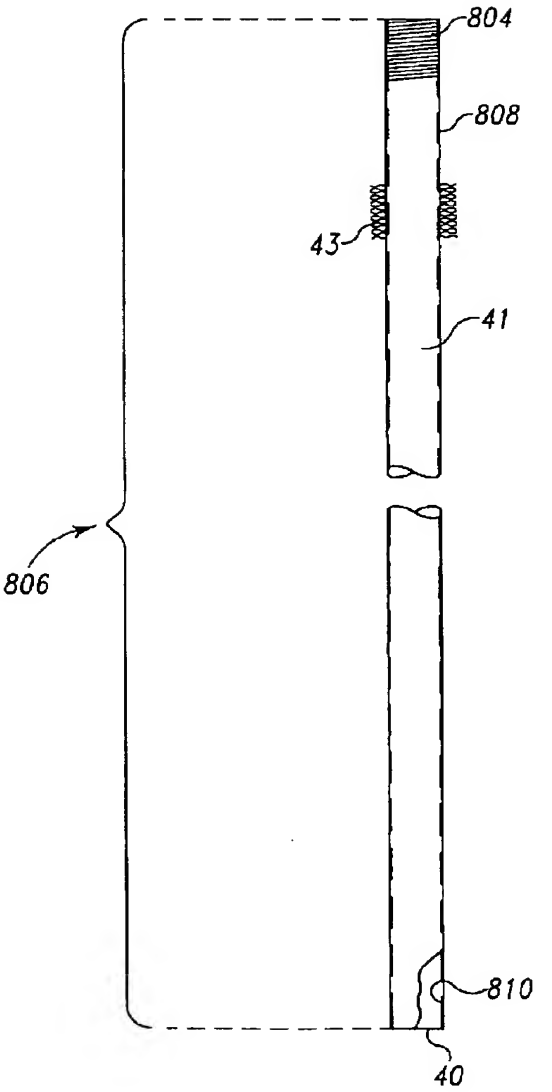

Fig. 36B

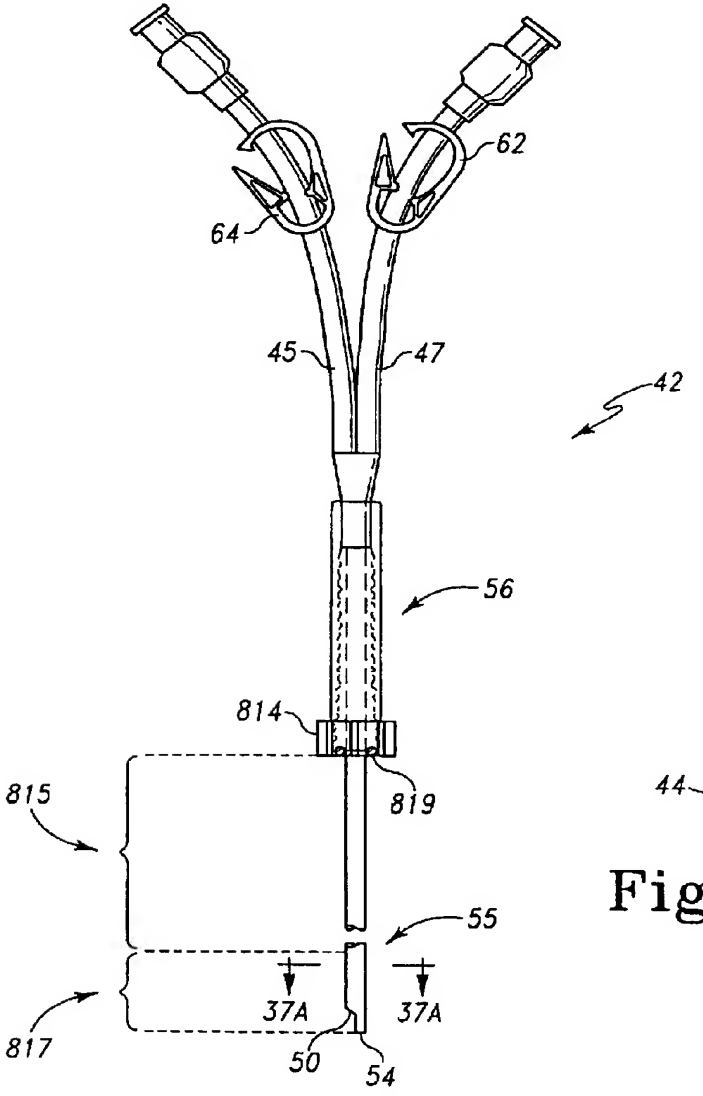

Fig. 37

Fig. 37A

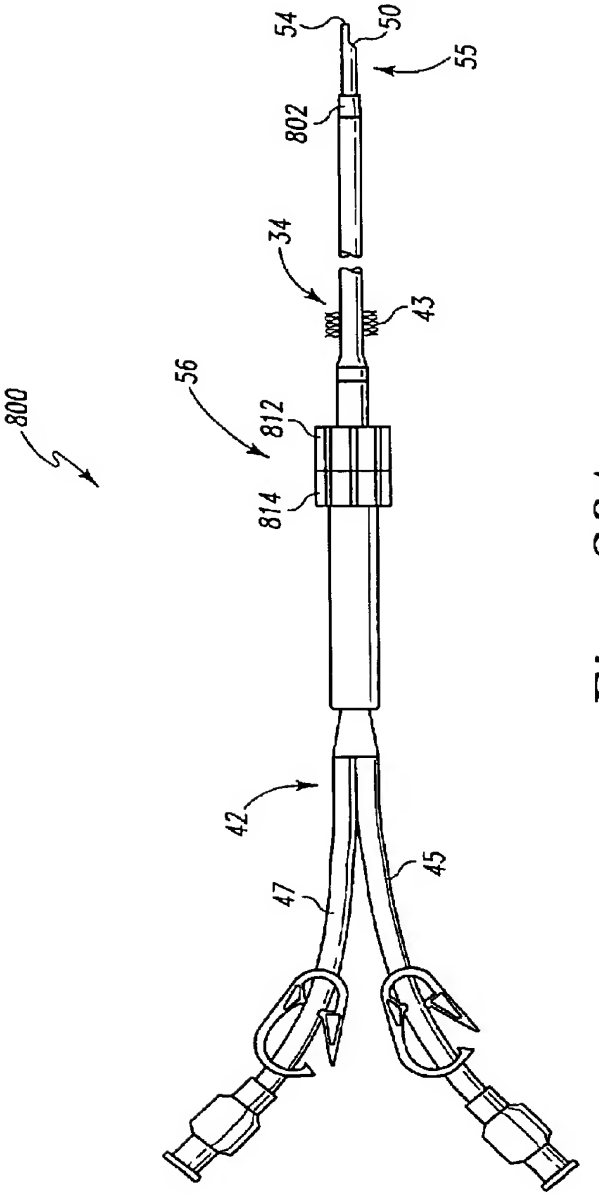

Fig. 38A

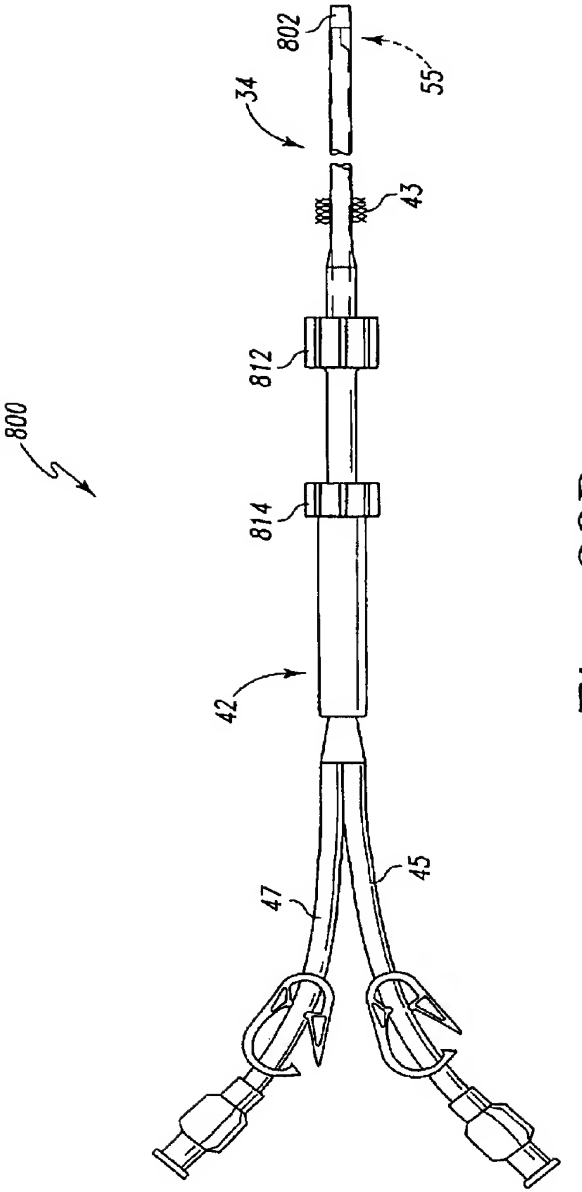

Fig. 38B

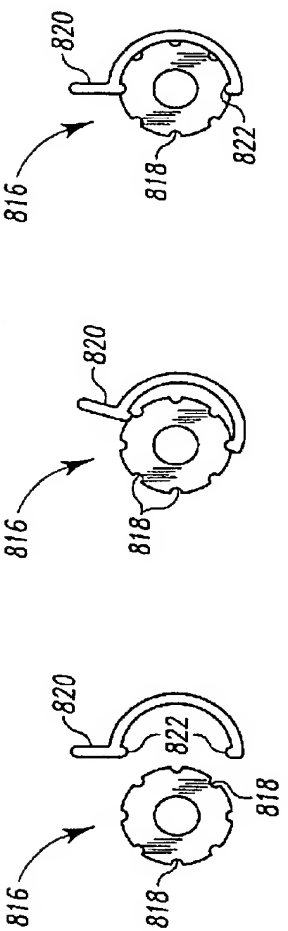

Fig. 39A

Fig. 39B

Fig. 39C

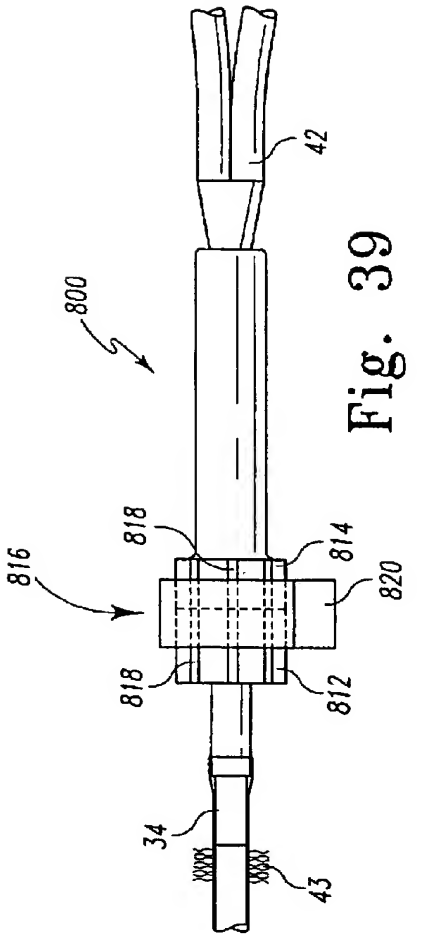

Fig. 39

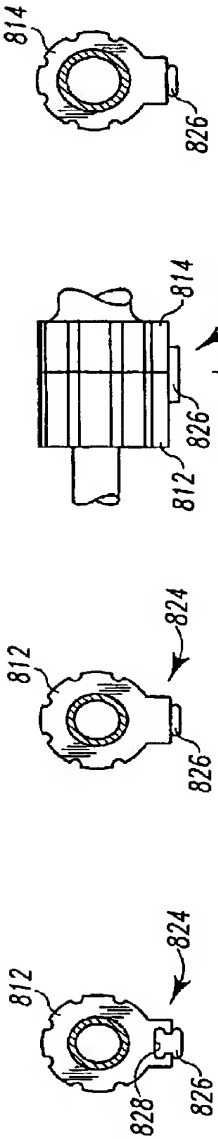

Fig. 40A

Fig. 40B

Fig. 40C

Fig. 40D

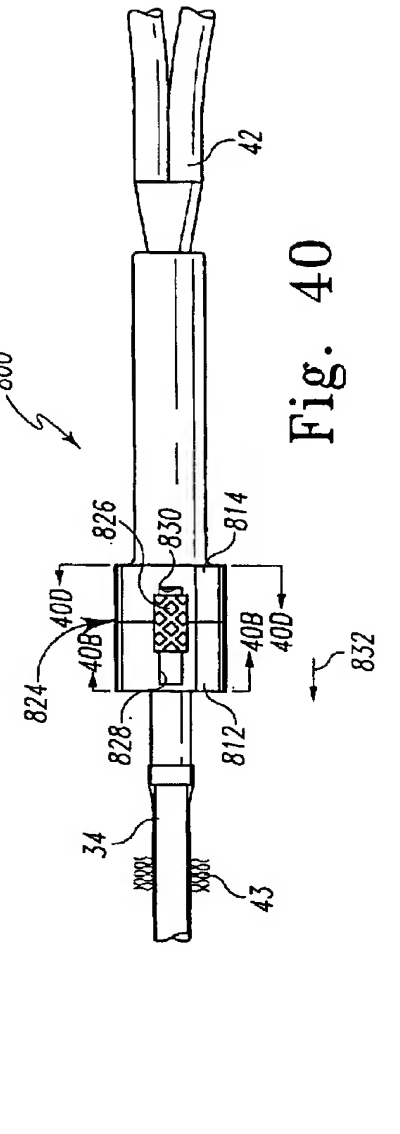

Fig. 40

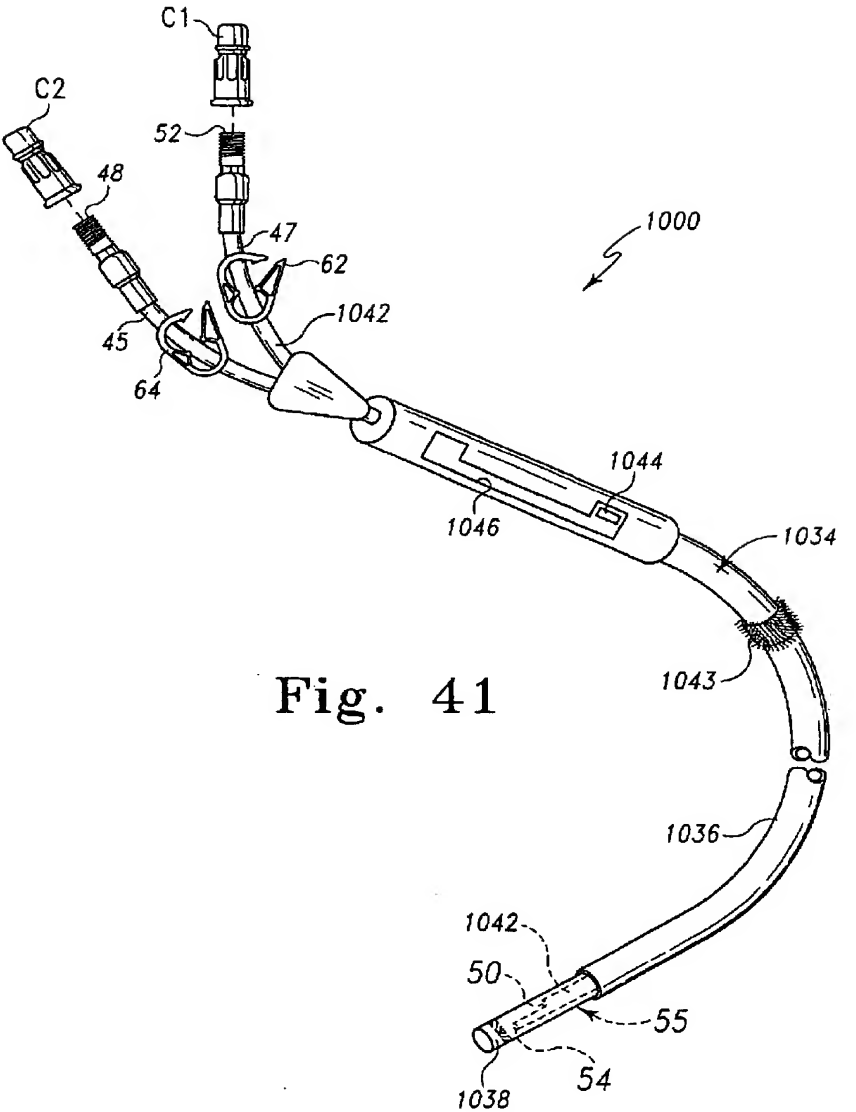
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Fig. 41

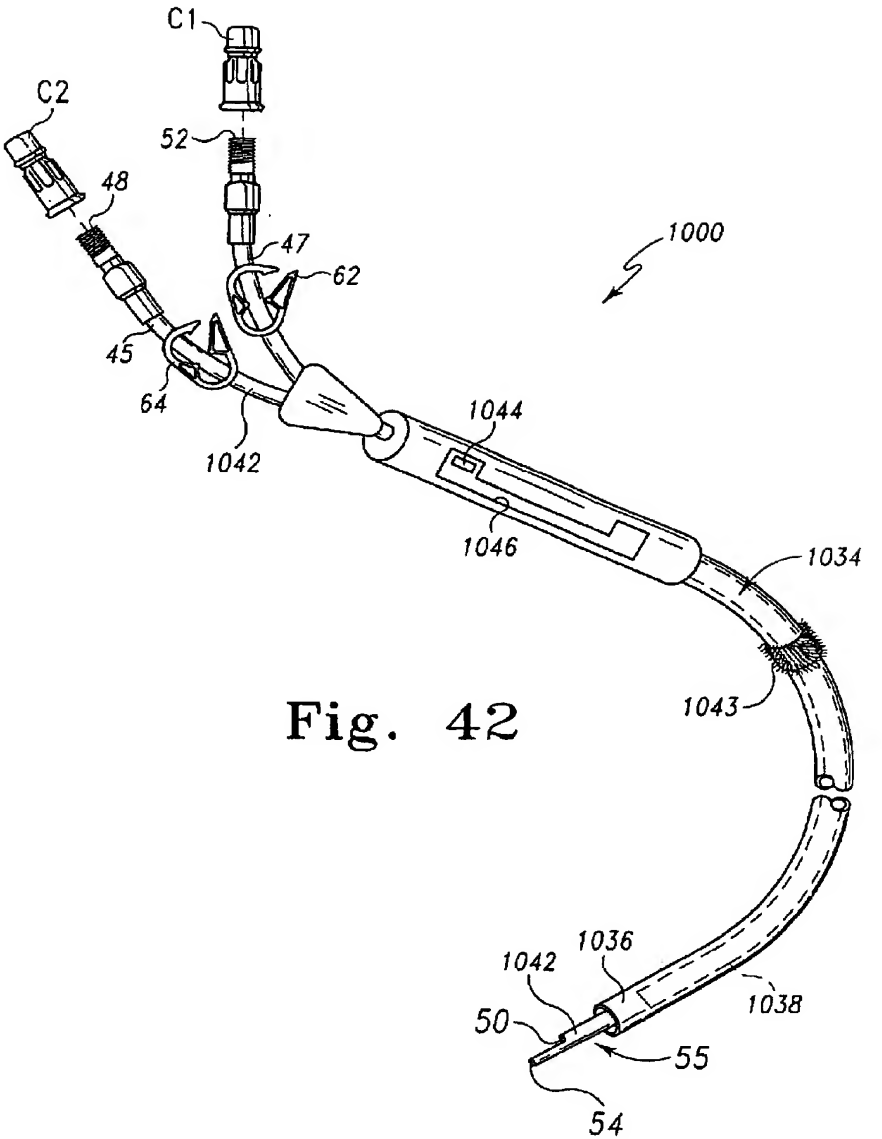
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Fig. 42

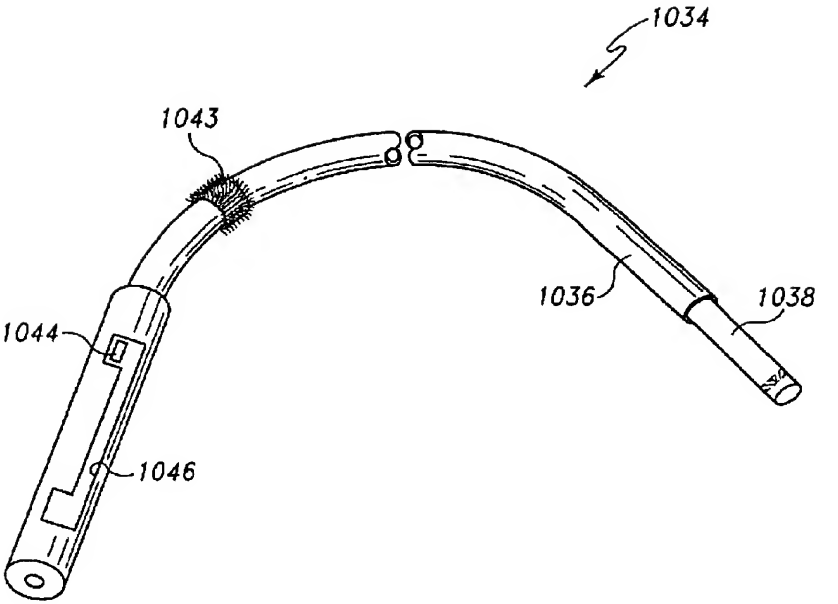

Fig. 43

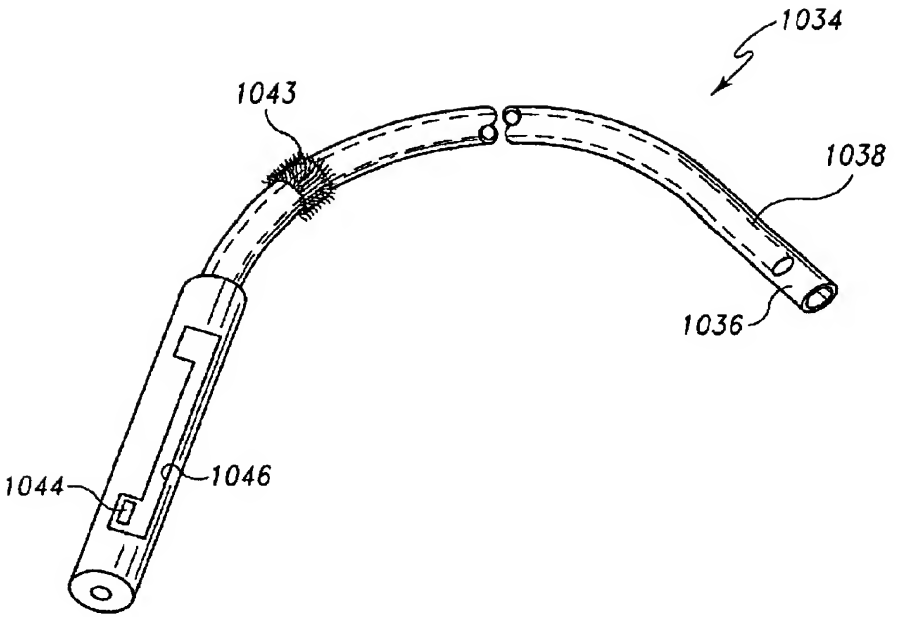

Fig. 44

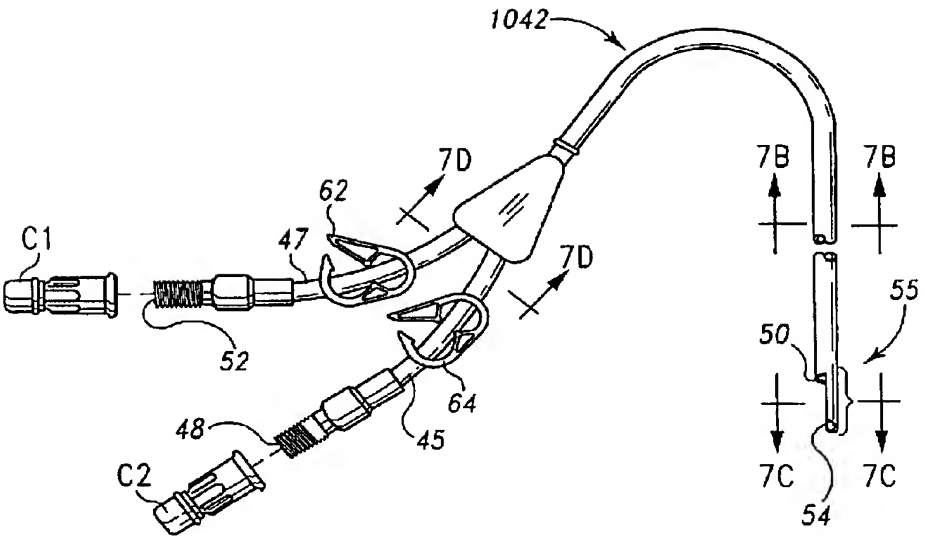

Fig. 45

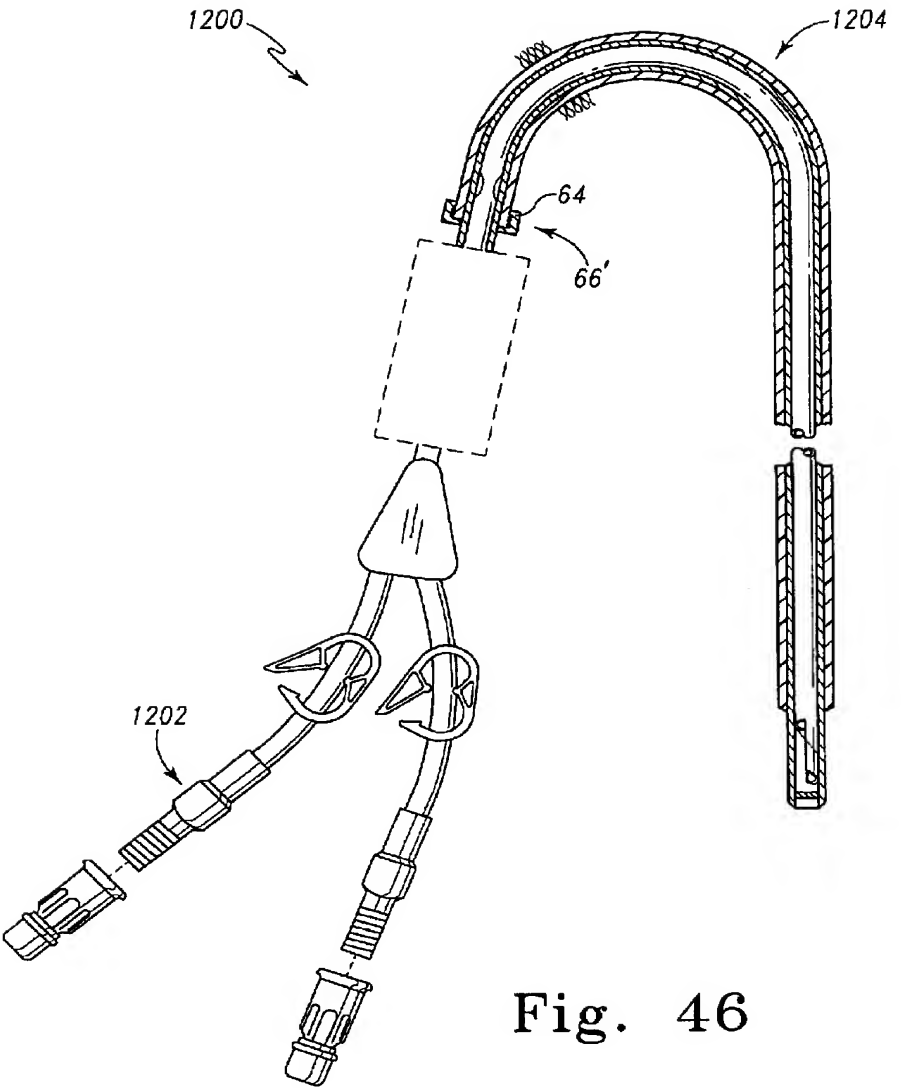

Fig. 46

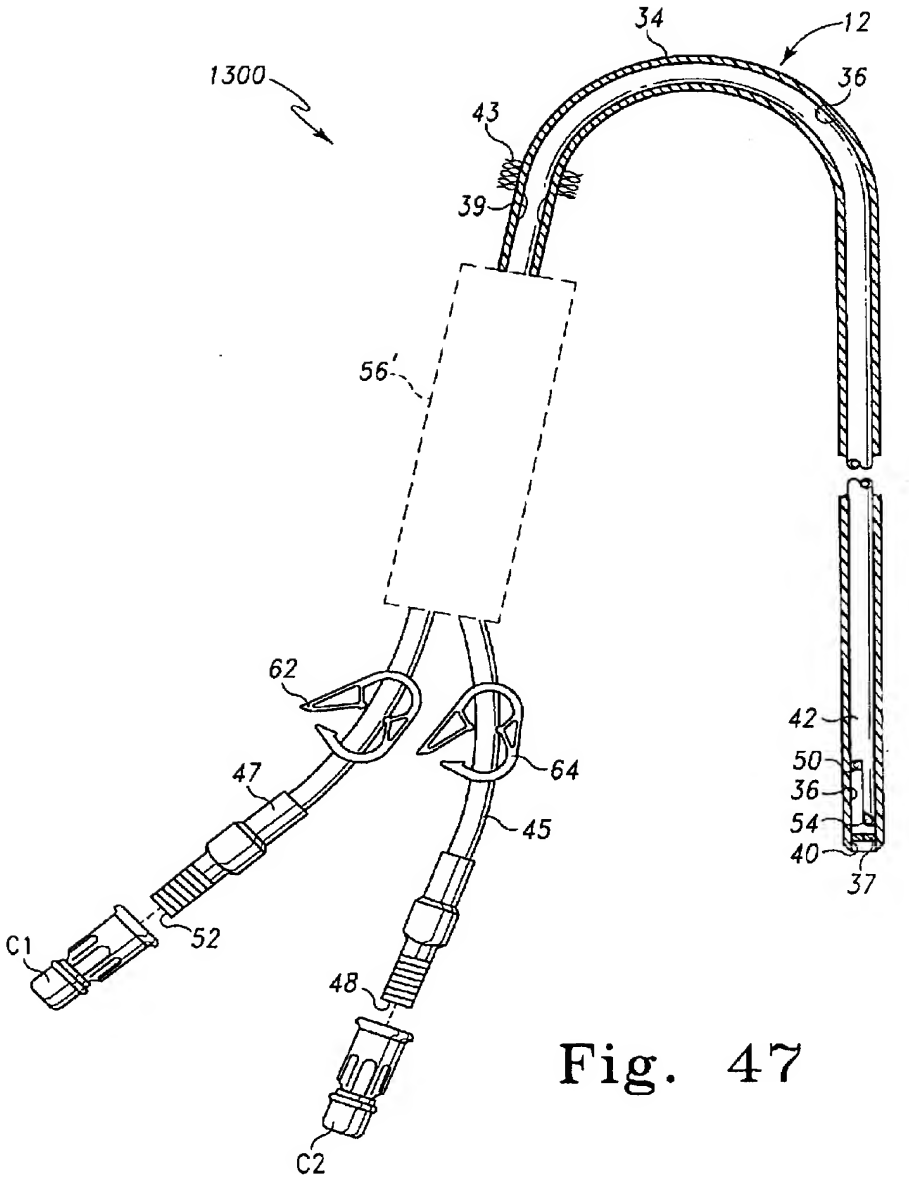

Fig. 47

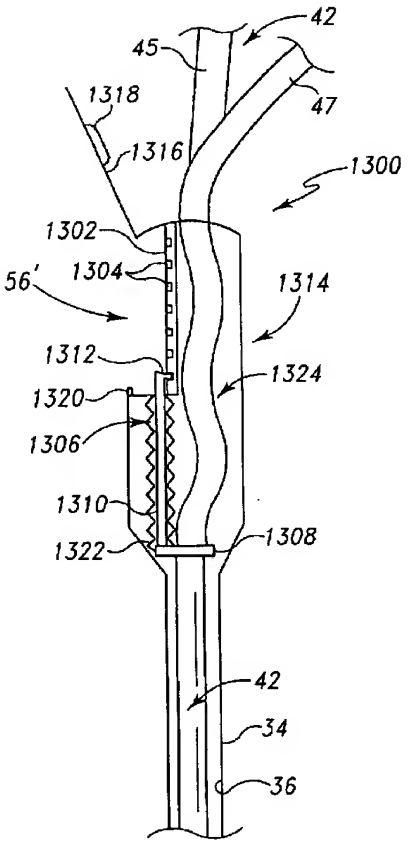
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Fig. 48

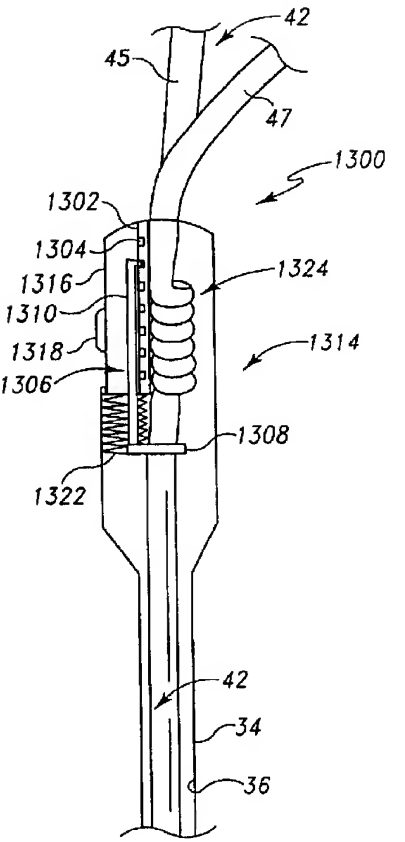
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Fig. 49

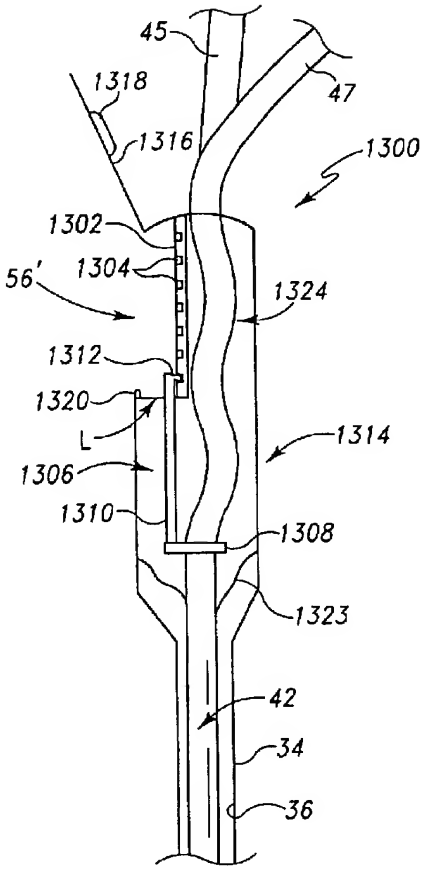
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Fig. 50

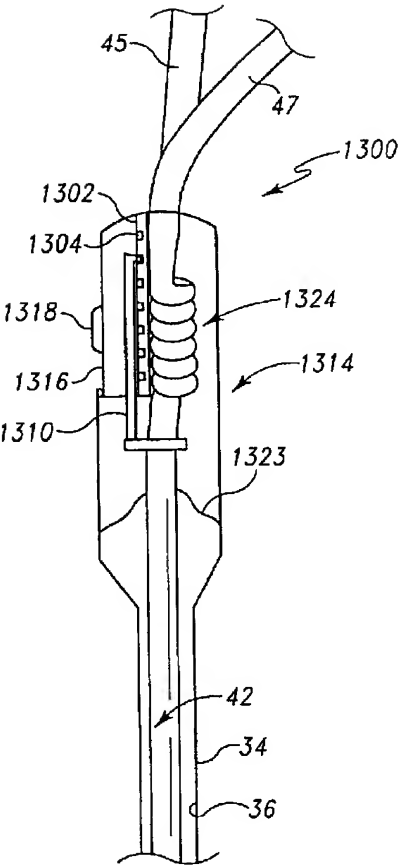
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Fig. 51

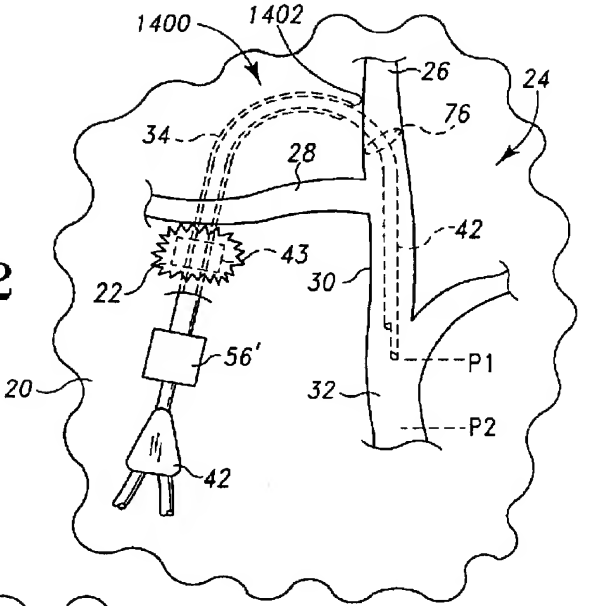
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Fig. 52

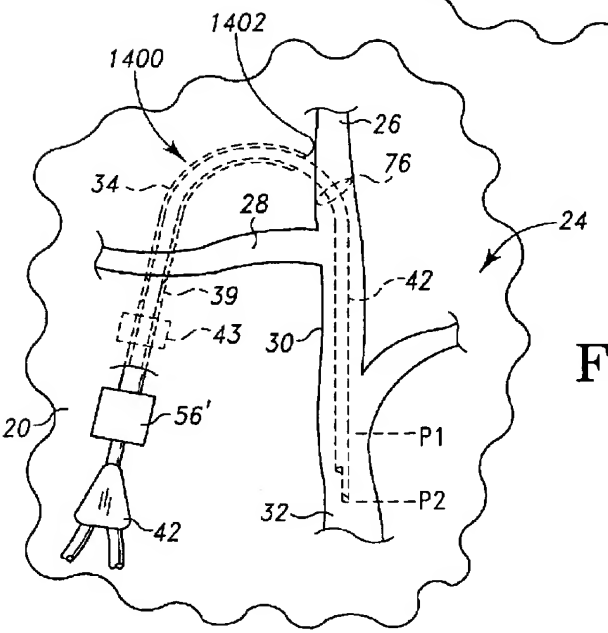
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Fig. 53

RETRACTABLE CATHETER SYSTEMS AND ASSOCIATED METHODS

This application is a continuation-in-part of both (i) application Ser. No. 09/716,815, filed on Nov. 20, 2000, and (ii) application Ser. No. 09/716,308, filed on Nov. 20, 2000, now U.S. Pat No. 6,585,705. Each of the above-identified patent applications Ser. Nos. 09/716,815 and 09/716,308 is a continuation-in-part of application Ser. No. 09/443,876, filed on Nov. 19, 1999, now U.S. Pat. No. 6,475,207 which in turn is a continuation-in-part of co-pending application Ser. No. 09/246,831, filed on Feb. 8, 1999, (now U.S. Pat. No. 6,190,371) which in turn claims the benefit of U.S. Provisional Application Serial No. 60/116,017, filed Jan. 15, 1999. The disclosures of each of the above-identified patent applications and patent being hereby totally incorporated by reference in their entirety.

CROSS REFERENCE

Cross reference is made to co-pending U.S. patent application Ser. No. 10/007,679 (Attorney Docket No.1537-0021), entitled "Subcutaneous Port Catheter System and Associated Method" by Thomas J. Maginot filed on the same date herewith, and co-pending U.S. patent application Ser. No. 10/005,277 (Attorney Docket No.1537-0022), entitled "Medical Procedure Using Catheter System having Removability Feature" by Thomas J. Maginot and Paul J. Maginot filed on the same date herewith, and co-pending U.S. patent application Ser. No. 09/716,814, entitled "Catheter Systems and Associated Methods having Removability Feature" by Thomas J. Maginot filed on Nov. 20, 2000, and also U.S. Pat. No. 6,156,016 issued to Maginot on Dec. 5, 2000, and also U.S. Pat. No. 5,989,213 issued to Maginot on Nov. 23, 1999. The disclosures of each of the above-identified patent applications and patents being hereby totally incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

The present invention relates generally to catheters, and more particularly to retractable catheter systems for use in a body of a patient and associated methods which maintain fluid flow in the catheter system.

Various medical procedures require that a patient be catheterized. For example, catheterization may be required when a patient undergoes hemodialysis or has a clot aspirated from a blood vessel. Generally, the length of time the patient will be catheterized dictates whether a physician will utilize a "temporary catheterization technique" (i.e. a technique in which the catheter is left in a blood vessel for a relatively short period of time such as a few minutes, hours, days, or weeks) or a "permanent catheterization technique" (i.e. a technique in which the catheter is left in a blood vessel for a relatively long period of time such as several months or indefinitely).

For example, a procedure in which a clot is aspirated from a blood vessel typically includes placing the catheter in the blood vessel for a relatively short period of time such as a few minutes to a few hours and then withdrawing the catheter once the clot has been removed. Therefore, when performing such an aspiration procedure, it is common for a physician to use the temporary catheterization technique to place the catheter in the blood vessel of the patient.

On the other hand, when a procedure is performed to effect hemodialysis, a physician may place a catheter in the blood vessel for a relatively long period of time. In particular, a patient suffering from kidney failure who is involved in a hemodialysis regimen typically requires a dialysis session three days per week for an indefinite period of time whereby extra fluid, chemicals, and wastes are removed from his/her body. A patient who is involved in such a hemodialysis regimen may need a catheter placed in his/her blood vessel for a relatively long period of time in order to provide a ready means for vascular access into his/her bloodstream over such relatively long period of time. This long term placement of the catheter for dialysis purposes may be desirable for a number of reasons.

Firstly, a patient may have experienced progressive loss of other conventional long term vascular access possibilities such as surgically created arteriovenous fistulas. Accordingly, the long term placement of the catheter in the patient's blood vessel may be the best alternative for the patient as he/she proceeds with the hemodialysis regimen.

Additionally, the long term placement of the catheter in the patient's blood vessel may be desirable after initial creation of an arteriovenous fistula in the patient's body. In particular, it is desirable to provide a ready means for vascular access into the patient's bloodstream during a maturation period of the arteriovenous fistula. The maturation period allows the arteriovenous fistula to develop sufficiently so that it will function as a ready means for vascular access into the patient's bloodstream which may be safely punctured multiple times per week for hemodialysis. The length of time of this maturation period is typically on the order of several weeks (e.g. three weeks) to many months (e.g. six months).

Therefore, when performing a hemodialysis procedure, it is common for a physician to use the permanent catheterization technique to place the catheter in the blood vessel of the patient.

These two catheterization techniques are significantly different with respect to their complexity and degree of invasiveness. For example, in the case of the temporary catheterization technique, it is common to insert a temporary catheter into a patient's blood vessel using a "direct puncture technique." This technique entails creating a small incision in a patient's skin with a scalpel directly over the blood vessel to be catheterized. A needle is then advanced through the skin incision and subcutaneous tissue and into the blood vessel. Thereafter, a guidewire is advanced through the needle into the blood vessel and the needle is subsequently removed over the guidewire. Then, one or more tubular vessel dilators are used to widen the opening defined in the skin and subcutaneous tissue, and further to widen the opening defined in the blood vessel wall to a caliber similar to that of the temporary catheter. The temporary catheter is then advanced over the guidewire and into the blood vessel. Thereafter, the guidewire is removed.

When the temporary catheterization technique is used during a clot aspiration procedure, two catheters are usually placed in the blood vessel of a patient. In particular, an outer catheter is usually placed within the blood vessel using the above described direct puncture technique so that its distal orifice is located near the clot. Thereafter, an inner catheter having a smaller caliber relative to the outer catheter is advanced through a lumen of the outer catheter. While the inner catheter is positioned within the outer catheter, an aspiration vacuum is applied to the inner catheter with a syringe. If the size of the clot (or fragments thereof) are smaller than the inner diameter of the inner catheter, then the clot or clot fragments are drawn into and through the inner catheter thereby removing the clot from the blood vessel. If the size of the clot or clot fragments are larger than the inner

diameter of the inner catheter, then the clot or clot fragments are drawn to a location adjacent to the distal orifice of the inner catheter. Subsequently, while the aspiration vacuum is still being applied, the inner catheter is withdrawn from the outer catheter thereby additionally withdrawing the clot or clot fragments from the outer catheter and the patient's blood vessel. Thereafter, the outer catheter remains temporarily in place within the blood vessel of the patient for subsequent injections of radiographic contrast for imaging purposes to determine the extent of clot remaining in the blood vessel as well as to determine if clot has migrated to another location within the blood vessel. The outer catheter, which remains temporarily in place in the blood vessel, provides a conduit for the inner catheter to be advanced back into the patient's blood vessel for additional aspiration attempts which are usually required for complete removal of the clot from the blood vessel.

If an outer catheter needs to be replaced during a clot aspiration procedure because of catheter malfunction, such replacement can be accomplished by advancing a guidewire through the lumen of the outer catheter and into the blood vessel. The existing outer catheter can then be removed over the guidewire to a location outside of the patient's body. Thereafter, a new outer catheter is placed in the patient's blood vessel by advancing the new outer catheter over the guidewire as discussed above.

In contrast to the temporary catheterization technique, the permanent catheterization technique typically entails inserting a permanent catheter into a patient's blood vessel using a "tunneled catheter technique." The tunneled catheter technique includes (i) creating a first opening by making a small incision in a patient's skin with a scalpel directly over the blood vessel to be catheterized, (ii) puncturing the blood vessel at a location directly below the first opening by advancing a needle through the skin incision and subcutaneous tissue and into the blood vessel, (iii) advancing a guidewire through the needle into the blood vessel, (iv) removing the needle over the guidewire, (v) passing one or more tubular vessel dilators over the guidewire to widen the opening defined in the skin and subcutaneous tissue, and further to widen the opening defined in the blood vessel wall to a caliber similar to that of the tubular guide, (vi) advancing the tubular guide over the guidewire and into the blood vessel, (vii) thereafter, creating a second opening in the patient's skin spaced apart at least several centimeters from the first opening, (viii) advancing a tunneling instrument from the second opening to the first opening so as to create a passageway within the subcutaneous tissue under the skin between the first opening and the second opening, (ix) advancing a permanent catheter having a tissue ingrowth member attached to an outer surface thereof into the second opening and through the passageway such that a distal end of the permanent catheter is located adjacent the first opening, (x) inserting the distal end of the permanent catheter through the tubular guide member and into the blood vessel to be catheterized whereby the tissue ingrowth member is positioned in the subcutaneous tissue, (xi) removing the tubular guide member, and (xii) closing the first opening with suture whereby the permanent catheter (a) is no longer exposed through the first opening, (b) extends for at least several centimeters under the patient's skin between the second opening and the location where the permanent catheter enters the blood vessel, and (c) extends out of the second opening so that a proximal end of the permanent catheter is located outside of the patient's body.

In contrast to the direct puncture catheter technique, the tunneled catheter technique results in the placement of a catheter in a patient's body in a manner which allows the catheter to remain safely in the patient's body for a relatively long period of time. For example, a degree of safety is achieved by separating the following two openings by at least several centimeters: (i) the skin opening through which the catheter enters the patient's body, and (ii) the blood vessel opening through which the catheter enters the patient's vascular system. This safety feature decreases the likelihood that bacteria will migrate up the length of the catheter from the skin opening and cause an infection at the blood vessel opening.

In addition, another degree of safety is achieved by providing a tissue ingrowth member which is attached to and extends around an outer surface of the catheter. As the catheter is left in the patient's body over a period of time, the tissue ingrowth member becomes affixed to the subcutaneous tissue of the patient's body thereby providing a secure attachment of the catheter to the patient's body. Providing a secure attachment between the catheter and the patient's body reduces the likelihood that the catheter will be inadvertently removed or withdrawn from the patient's body. Moreover, since the subcutaneous tissue becomes attached to the tissue ingrowth member, a physical barrier is created between following two openings: (i) the skin opening through which the catheter enters the patient's body, and (ii) the blood vessel opening through which the catheter enters the patient's vascular system. This physical barrier further decreases the likelihood that bacteria will migrate up the length of the catheter from the skin opening and cause an infection at the blood vessel opening.

While the tunneled catheter technique provides the significant advantage of allowing the catheter to remain safely in the patient's body for a relatively long period of time, significant disadvantages of the tunneled catheter technique exists. For example, when a catheter remains in a blood vessel for a long period of time, there is a tendency for blood clots including fibrin (e.g. in the form of a fibrin sheath) to attach to and build-up on the outer and inner surfaces of the portion of the catheter which is located within the blood vessel. The above described attachment and build-up tends to occlude the various distal orifices defined in the catheter which enable fluid movement into and out of the catheter. For instance, attempts at withdrawing blood through the catheter may be unsuccessful due to blood clots creating a "ball-valve" effect which occlude the various distal orifices of the catheter.

When occlusion of the various distal orifices of the catheter occurs due to the above described blood clot attachment and build-up, a physician has several options for eliminating the occlusion thereby reestablishing access to the vascular system. One option is to remove the occluded catheter and replace it with a new catheter. However, in contrast to the ease of exchanging a catheter which was placed in the patient's body using the direct puncture technique, exchanging a catheter which was placed in the patient's body using the tunneled catheter technique is substantially more complicated and invasive. This is true since in order to remove the occluded catheter from the patient's body, the physician must surgically dissect the tissue ingrowth member which is secured to the outer surface of the catheter from the patient's subcutaneous tissue. Recall that the tissue ingrowth member becomes affixed to the subcutaneous tissue over a period of time. Thereafter, the physician would place a new catheter into the patient's body generally using the above described tunneled catheter technique. Thus, this option is undesirable since it requires additional surgery which further traumatizes the patient and increases the cost of the medical care.

Another option for eliminating the occlusion of the various distal orifices of the catheter in order to reestablish access to the vascular system involves the performance of a medical procedure in which a blood clot-dissolving medication such as urokinase is infused into the catheter. However, this medication is not always successful in eliminating the occlusion of the various distal orifices of the catheter. In addition, infusion of the medication into the catheter subjects the patient to potential bleeding complications due to the medication entering the vascular system and being circulated systemically. Further, this medication is expensive. Thus, this option has serious drawbacks as well.

An additional option for eliminating the occlusion of the various distal orifices of the catheter in order to reestablish access to the vascular system involves the performance of a medical procedure in which an intravascular snare is introduced into the blood vessel in order to physically strip off any blood clots or fibrin sheath which has attached and built-up on the distal portion of the catheter. However, for catheters placed in veins, this medical procedure requires a venopuncture in the femoral or jugular vein which is invasive and can be uncomfortable for a patient. Furthermore, this option requires the use of (i) an intravascular snare, (ii) a physician experienced in catheter techniques, and (iii) an angiographic suite to provide fluoroscopic imaging. Use of each of items (i), (ii), and (iii) above causes this option to be relatively expensive. Consequently, this option also has significant disadvantages.

What is needed therefore is a method and apparatus which reduces the likelihood of occlusion of the various distal orifices of a catheter which has been placed in a patient's body using the tunneled catheter technique which overcomes one or more of the above-mentioned drawbacks. What is also needed is an improved long-term catheter system and associated method of maintaining fluid flow in the catheter system.

SUMMARY OF THE INVENTION

In accordance with one embodiment of the present invention, there is provided a catheter system which includes a working catheter having a distal working orifice. The catheter system further includes a guide catheter having a guide lumen and a distal guide orifice. The catheter system additionally includes a locking mechanism which locks the working catheter relative to the guide catheter in (i) an operative position, and (ii) a stowed position. When the working catheter is locked in the operative position, (i) the working catheter extends through the guide lumen of the guide catheter and out of the distal guide orifice of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned outside of the guide catheter. When the working catheter is locked in the stowed position, (i) the working catheter extends into the guide lumen of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned within the guide lumen of the guide catheter.

Pursuant to another embodiment of the present invention, there is provided a method of performing dialysis with a catheter system which includes (i) a working catheter having a distal working orifice, and (ii) a guide catheter having a guide lumen and a distal guide orifice. The method includes the step of locking the working catheter in an operative position in which (i) the working catheter extends through the guide lumen of the guide catheter and out of the distal guide orifice of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned outside of the guide catheter. The method further includes the step of advancing and withdrawing blood through the working catheter while the working catheter is locked in the operative position. Also, the method includes the step of locking the working catheter in a stowed position in which (i) the working catheter extends into the guide lumen of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned within the guide lumen of the guide catheter.

According to still another embodiment of the present invention, there is provided a method of performing a medical procedure with a catheter system which includes (i) a working catheter having a distal working orifice, and (ii) a guide catheter having a guide lumen and a distal guide orifice. The method includes the step of locking the working catheter in an operative position in which (i) the working catheter extends through the guide lumen of the guide catheter and out of the distal guide orifice of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned outside of the guide catheter. Moreover, the method includes the step of advancing and withdrawing fluid through the working catheter while the working catheter is locked in the operative position. The method also includes the step of locking the working catheter in a stowed position in which (i) the working catheter extends into the guide lumen of the guide catheter, and (ii) the distal working orifice of the working catheter is positioned within the guide lumen of the guide catheter.

In accordance with yet another embodiment of the present invention, there is provided a catheter system which includes a multi-lumen working catheter having a first distal working orifice and a second distal working orifice. The catheter system further includes a guide catheter having a guide lumen and a distal guide orifice. Also, the catheter system includes a locking mechanism which locks the working catheter relative to the guide catheter in (i) an operative position, and (ii) a stowed position. When the working catheter is locked in the operative position, (i) the working catheter extends through the guide lumen of the guide catheter and out of the distal guide orifice of the guide catheter, and (ii) the first distal working orifice and the second distal working orifice are each positioned outside of the guide catheter. Additionally, when the working catheter is locked in the stowed position, (i) the working catheter extends into the guide lumen of the guide catheter, and (ii) the first distal working orifice and the second distal working orifice are each positioned within the guide lumen of the guide catheter.

It is therefore an object of the present invention to provide a new and useful catheter system for use in a body of a patient.

It is also an object of the present invention to provide a new and useful long-term catheter system for use in a body of a patient.

It is another object of the present invention to provide an improved longterm catheter system for use in a body of a patient.

It is yet another object of the present invention to provide a new and useful method of performing dialysis with a catheter system.

It is still another object of the present invention to provide an improved method of performing dialysis with a catheter system.

Other objects and benefits of the present invention can be discerned from the following description and accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a perspective view of a patient undergoing a dialysis procedure utilizing the catheter system of the present invention;

FIG. **2** is a schematic view of a portion of the vascular system of the patient of FIG. **1**, showing the right internal jugular vein, the right subclavian vein, the right innominate vein, and the superior vena cava;

FIG. **3** is an enlarged side elevational view of the catheter system of FIG. **1**, showing the working catheter positioned within the guide lumen of the guide catheter, and further schematically showing the locking mechanism which is configured to lock the working catheter relative to the guide catheter in any one of a plurality of positions (note that FIG. **3** shows the locking mechanism operating to lock the working catheter in the stowed position);

FIG. **4** is a view similar to FIG. **3** but showing one example of a locking mechanism which can be used in the present invention (note that FIG. **4** shows the locking mechanism operating to lock the working catheter in the stowed position);

FIG. **5** is a view similar to FIG. **4** but showing the locking mechanism operating to lock the working catheter in the operative position;

FIG. **6**A is an enlarged side elevational view of the guide catheter of the catheter system shown in FIG. **1**;

FIG. **6**B is an enlarged fragmentary cross sectional view of the guide catheter taken along the line **6**B—**6**B of FIG. **6**A as viewed in the direction of the arrows;

FIG. **6**C is an enlarged cross sectional view of the guide catheter taken along the line **6**C—**6**C of FIG. **6**A as viewed in the direction of the arrows;

FIG. **6**D is an enlarged cross sectional view of the guide catheter taken along the line **6**D—**6**D of FIG. **6**A as viewed in the direction of the arrows;

FIG. **7**A is an enlarged side elevational view of the working catheter of the catheter system shown in FIG. **1**;

FIG. **7**B is an enlarged cross sectional view of the working catheter taken along the line **7**B—**7**B of FIG. **7**A as viewed in the direction of the arrows;

FIG. **7**C is an enlarged cross sectional view of the working catheter taken along the line **7**C—**7**C of FIG. **7**A as viewed in the direction of the arrows;

FIG. **7**D is an enlarged cross sectional view of the working catheter taken along the line **7**D—**7**D of FIG. **7**A as viewed in the direction of the arrows;

FIG. **8** is an enlarged view of a portion of FIG. **5** which shows the locking mechanism of FIG. **5** in more detail;

FIG. **8**A is also an enlarged view of a portion of FIG. **5** which shows the locking mechanism of FIG. **5** in more detail, however, FIG. **8**A shows a separating diaphragm being used in place of the proximal valve;

FIG. **9** is an enlarged view which is similar to FIG. **2**, but showing the catheter system of FIG. **1** (i) extending from the right upper chest, (ii) tunneled under the skin within the subcutaneous tissue of the patient for a distance, (iii) entering a venotomy in the right internal jugular vein, and (iv) passing caudally in the right internal jugular vein, the right innominate vein and the superior vena cava;

FIG. **10** is a fragmentary enlarged view which is similar to FIG. **9**, but showing the working catheter locked to the guide catheter in the stowed position;

FIG. **11** is a view similar to FIG. **10**, but showing the working catheter locked to the guide catheter in the operative position;

FIG. **12** is a view similar to FIG. **3**, but showing another catheter system which incorporates the features of the present invention therein, with the working catheter shown positioned in the operative position;

FIG. **13** is a fragmentary cross sectional view of a distal portion of the catheter system of FIG. **12**, but showing the working catheter positioned in the stowed position;

FIG. **14** is a view similar to FIG. **3**, but showing yet another catheter system which incorporates the features of the present invention therein, with the working catheters shown positioned in the operative position;

FIG. **15** is a fragmentary cross sectional view of a distal portion of the catheter system of FIG. **14**, but showing the working catheters positioned in the stowed position;

FIG. **16** is a view similar to FIG. **14**, but showing another catheter system which incorporates the features of the present invention therein, with the working catheters shown positioned in the operative position;

FIG. **17** is a view similar to FIG. **3**, but showing another catheter system which incorporates the features of the present invention therein, with the working catheter shown positioned in the operative position;

FIG. **18** is a fragmentary cross sectional view of a distal portion of the catheter system of FIG. **17**, but showing the working catheter positioned in the stowed position;

FIG. **19** is a view similar to FIG. **17**, but showing another catheter system which incorporates the features of the present invention therein, with the working catheter shown positioned in the operative position;

FIG. **20** is a view similar to FIG. **17**, but showing still another catheter system which incorporates the features of the present invention therein;

FIG. **21** is a view similar to FIG. **3**, but showing yet another catheter system which incorporates the features of the present invention therein, with the working catheters shown positioned in the operative position;

FIG. **22** is a fragmentary cross sectional view of a distal portion of the catheter system of FIG. **21**, but showing the working catheters positioned in the stowed position;

FIG. **23** is an enlarged view which is similar to FIG. **2**, but showing the catheter system of FIG. **21** (i) extending from the right upper chest, (ii) tunneled under the skin within the subcutaneous tissue of the patient for a distance, (iii) entering a pair of venotomies in the right internal jugular vein, and (iv) passing caudally in the right internal jugular vein, the right innominate vein and the superior vena cava;

FIG. **24** is a view similar to FIG. **3**, but showing still another catheter system which incorporates the features of the present invention therein, with the working catheter shown positioned in the operative position;

FIG. **25** is a fragmentary cross sectional view of a distal portion of the catheter system of FIG. **24**, but showing the working catheter positioned in the stowed position;

FIG. **26** is an enlarged view which is similar to FIG. **2**, but showing the catheter system of FIG. **24** (i) extending from the right upper chest, (ii) tunneled under the skin within the subcutaneous tissue of the patient for a distance, (iii) entering a venotomy in the right internal jugular vein, and (iv) passing caudally in the right internal jugular vein, the right innominate vein and the superior vena cava;

FIG. **27** is a view similar to FIG. **24**, but showing another catheter system which incorporates the features of the present invention therein, with the working catheter shown positioned in the operative position;

FIG. **28** is an enlarged perspective view of the closure member of FIG. **27**;

FIG. **29** is an enlarged cross sectional view of the closure member of FIG. **28** taken along the line **29**—**29** of FIG. **28** as viewed in the direction of the arrows;

FIG. **30** is a side elevational view showing another catheter system which incorporates the features of the present invention therein, with the catheter system shown in the retracted or stowed position; and

FIG. **31** is a view similar to FIG. **51**, but showing the catheter system of FIG. **30** being positioned in the extended or operative position;

FIG. **32** is a view similar to FIG. **24**, but showing another catheter system which incorporates the features of the present invention therein, and showing the tube segment positioned in the stowed position;

FIG. **33** is a view similar to FIG. **32**, but showing the tube segment positioned in the operative position;

FIG. **34** is a perspective view of the tube segment of the retractable conduit assembly of FIG. **35**;

FIG. **35** is a side elevational view of the retractable conduit assembly of the catheter system of FIG. **32**;

FIG. **36** is an enlarged side elevational view of the guide catheter of the long-term dialysis catheter system shown in FIG. **38A**;

FIG. **36A** is an enlarged cross sectional view of the guide catheter taken along the line **36A**—**36A** of FIG. **36** as viewed in the direction of the arrows;

FIG. **36B** is an enlarged side elevational view of a portion of the guide catheter of FIG. **36**;

FIG. **37** is an enlarged side elevational view of the working catheter of the long-term dialysis catheter system shown in FIG. **38A**;

FIG. **37A** is an enlarged cross sectional view of the guide catheter taken along the line **37A**—**37A** of FIG. **37** as viewed in the direction of the arrows;

FIG. **38A** is a view similar to FIG. **3**, but showing another catheter system which incorporates the features of the present invention therein, with the working catheter shown positioned in the operative position;

FIG. **38B** is a view similar to FIG. **38A**, but showing the working catheter positioned in the stowed position;

FIG. **39** is an enlarged fragmentary elevational view of the catheter system of FIG. **38A** showing a supplemental locking system;

FIGS. **39A**, **39B**, and **39C** are various views of the locking clip of the supplemental locking system of FIG. **39** being applied over the finger grips;

FIG. **40** is an enlarged fragmentary elevational view of the catheter system of FIG. **38A** showing an alternative supplemental locking system; and

FIG. **40A** is an enlarged cross sectional view of the first finger grip and slider taken along the line **40A**—**40A** of FIG. **40C** as viewed in the direction of the arrows (Note that the dialysis catheter is shown removed for clarity of description);

FIG. **40B** is an enlarged cross sectional view of the first finger grip and slider taken along the line **40B**—**40B** of FIG. **40** as viewed in the direction of the arrows (Note that the dialysis catheter is shown removed for clarity of description);

FIG. **40C** is enlarged fragmentary elevational view of the catheter system of FIG. **40** showing an alternative view of the first and second finger grips;

FIG. **40D** is an enlarged cross sectional view of the second finger grip and slider taken along the line **40D**—**40D** of FIG. **40** as viewed in the direction of the arrows (Note that only the second finger grip and slider is shown for clarity of description);

FIG. **41** is a view similar to FIG. **3**, but showing another catheter system which incorporates the features of the present invention, with the catheter system being shown in a stowed position;

FIG. **42** is a view similar to FIG. **41**, but showing the catheter system being shown in a operative position;

FIG. **43** is a side elevational view of the retractable sheath assembly of the catheter system of FIG. **41**, and showing the inner retractable conduit extending outside of the outer guide tube;

FIG. **44** is a view similar to FIG. **43**, but showing the inner retractable conduit positioned within the outer guide tube;

FIG. **45** is an elevational view of the working catheter of the catheter system of FIG. **41**;

FIG. **46** is a side elevational view of another catheter system that incorporates the features of the present invention therein;

FIG. **47** is a side elevational view of still another catheter system that incorporates the features of the present invention therein;

FIGS. **48**, **49**, **50**, and **51** are views similar to FIG. **47**, but showing more details of the locking mechanism of FIG. **47**;

FIGS. **52** and **53** are views similar to FIGS. **10** and **11**, but showing yet another catheter system that incorporates the features of the present invention therein. Note that FIG. **52** shows the working catheter locked to the guide catheter in its retracted position, while FIG. **53** shows the working catheter locked to the guide catheter in its retracted position.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

While the invention is susceptible to various modifications and alternative forms, specific embodiments thereof have been shown by way of example in the drawings and will herein be described in detail. It should be understood, however, that there is no intent to limit the invention to the particular forms disclosed, but on the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

I. Catheter System **12**

Referring now to FIG. **1**, there is shown a hemodialysis machine **10** to which is attached a long-term catheter system **12** which incorporates the features of the present invention therein. The catheter system **12** is inserted in a patient's body **14**. The hemodialysis machine **10** includes an inlet line **16** and an outlet line **18** which are each in fluid communication with the catheter system **12**. The body **14** includes skin, generally indicated by the reference numeral **20**. The body **14** further includes subcutaneous tissue **22** positioned below the skin **20** (see e.g. FIG. **9**).

As shown in FIG. **2**, the body **14** further includes a vascular system **24**. The vascular system **24** includes a right internal jugular vein **26**, a right subclavian vein **28**, a right innominate vein **30**, and a superior vena cava **32**. Note that the vascular system **24** is positioned within the body **14** underneath the skin **20**. However, the vascular system **24**, including the right internal jugular vein **26**, the right subclavian vein **28**, the right innominate vein **30**, and the superior vena cava **32**, are depicted in FIGS. **2**, **9**–**11**, **23**, and **26** with solid lines for clarity of description.

The catheter system **12** is shown in more detail in FIG. **3**. In particular, the catheter system includes a guide catheter **34** having a central guide lumen **36** which extends the entire length thereof (see also FIGS. **6A–6D**). The guide lumen **36** defines a proximal guide orifice **38** and a distal guide orifice **40**.

A distal valve **37** is secured to the guide catheter **34** at a location within the guide lumen **36** substantially adjacent to the distal guide orifice **40** (see e.g. FIGS. **3–5**, **6A** and **6C**). The distal valve **37** is configured to inhibit fluid from advancing through the distal guide orifice **40** and past the distal valve **37** within the guide lumen **36** of the guide catheter **34**. A proximal valve **39** is also secured to the guide catheter **34** at a location within the guide lumen **36** (see also FIGS. **6A**, **6B**, and **8**). The proximal valve **39** is configured to inhibit fluid from advancing within the guide lumen **36** from one side of the proximal valve **39** to the other side of the proximal valve **39**. The valves **37**, **39** also function to inhibit air flow leakage though the guide lumen **36** of the guide catheter **34**. One valve which may be used as either the distal valve **37** or the proximal valve **39** with some modifications is available from Micro Therapeutics, Inc. of San Clemente, Calif. under the trademark "Cragg MicroValve™".

Alternatively, a flexible separating diaphragm **39A** may be substituted for the proximal valve **39** as shown in FIG. **8A**. The separating diaphragm **39A** would have a first end thereof secured to the inner surface of the guide catheter **34**, and a second end thereof secured to the outer surface of the working catheter **42** as shown in FIG. **8A**. The first end of the separating diaphragm **39A** would be secured to an entire 360° segment of the inner surface of the guide catheter **34** whereby fluid is completely prevented from advancing between the separating diaphragm **39A** and the guide catheter **34**. Similarly, the second end of the separating diaphragm **39A** would be secured to an entire 360° segment of the outer surface of the working catheter **42** whereby fluid is completely prevented from advancing between the separating diaphragm **39A** and the working catheter **42**. Accordingly, fluid is completely prevented from advancing within the guide lumen **36** of the guide catheter **34** from one side of the separating diaphragm **39A** to the other side of the separating diaphragm **39A**. The separating diaphragm **39A** also functions to prevent air flow leakage though the guide lumen **36** of the guide catheter **34**. The separating diaphragm **39A** is made from the same material from which the proximal valve **39** is made.

Referring again to FIGS. **6A–6D**, the guide catheter **34** also includes an outer surface **41** having a tissue ingrowth member **43** secured thereto. The tissue ingrowth member **43** is configured to facilitate fibrous tissue growth therein. More specifically, the subcutaneous tissue **22** of the body **14** becomes affixed to the tissue ingrowth member **43** when the tissue ingrowth member **43** remains in contact with the subcutaneous tissue **22** over a period of time. One type of tissue ingrowth member which may be used as the tissue ingrowth member **43** is a DACRON cuff which is available from Bard Access Systems of Salt Lake City, Utah.

The catheter system **12** further includes a working catheter **42** which is positioned within the guide lumen **36** of the guide catheter **34** (see FIGS. **3–5** and **10–11**). The working catheter **42** has an ingress lumen **44** through which fluid may be advanced, and an egress lumen **46** also through which fluid may be advanced (see FIGS. **7A–7D**). The ingress lumen **44** defines a first distal working orifice **50**, while the egress lumen **46** defines a second distal working orifice **54**. The first distal working orifice **50** and the second distal working orifice **54** are defined in a distal working segment **55** of the working catheter **42** (see FIGS. **4**, **5**, and **7A**).

The working catheter **42** further includes an ingress line **45** and an egress line **47**. The ingress line **45** defines a first proximal working orifice **48**, while the egress line **47** defines a second proximal working orifice **52**. The ingress line **45** is in fluid communication with the ingress lumen **44**, while the egress line **47** is in fluid communication with the egress lumen **46**. The egress line **47** has an adapter or injection cap **C1** attached thereto, and the ingress line **45** has an adapter or injection cap **C2** attached thereto (see FIG. **7A**).

In addition, a clamp **62** is positioned on the egress line **47**, while a clamp **64** is positioned on the ingress line **45** as shown in FIG. **7A**. It should be understood that closure of the clamp **64** causes fluid communication between the first proximal working orifice **48** and the first distal working orifice **50** to be prevented. Similarly, closure of the clamp **62** prevents fluid communication between the second proximal working orifice **52** and the second distal working orifice **54**.

The catheter system **12** additionally includes a locking mechanism **56** which is schematically shown in FIG. **3**. The locking mechanism **56** operates to lock the working catheter **42** in relation to the guide catheter **34** at any one of two positions. In particular, the locking mechanism **56** may lock the working catheter **42** relative to the guide catheter **34** in an operative position (see e.g. FIGS. **5**, **9**, and **11**) or in a stowed position (see e.g. FIGS. **3**, **4** and **10**). It should be noted that when the working catheter **42** is locked in the operative position, (i) the working catheter **42** extends through the guide lumen **36** of the guide catheter **34** and out of the distal guide orifice **40** of the guide catheter **34**, and (ii) the first distal working orifice **50** and the second distal working orifice **54** are each positioned outside of the guide catheter **34**. On the other hand, when the working catheter **42** is locked in the stowed position, (i) the working catheter **42** extends into the guide lumen **36** of the guide catheter **34**, and (ii) the first distal working orifice **50** and the second distal working orifice **54** are each positioned within the guide lumen **36** of the guide catheter **34**.

One type of locking mechanism which may be used as the locking mechanism **56** of the present invention is shown in more detail in FIGS. **4**, **5**, **6A**, **6B**, **7A**, and **8**. Reference number **56** will also be used to identify this locking mechanism. In particular, the locking mechanism **56** includes an internally threaded member **66**. The internally threaded member **66** is attached to the guide catheter **34** in a manner which allows the internally threaded member to rotate relative to the guide catheter **34** (see FIGS. **6B** and **8**).

The locking mechanism **56** further includes a first set of external threads **68** and a second set of external threads **70** which are each defined in an exterior surface of the working catheter **42**. As shown in FIG. **8**, the first set of external threads **68** is spaced apart from the second set of external threads **70**. The internally threaded member **66** meshes with the first set of external threads **68** so as to lock the working catheter **42** in the operative position as shown in FIG. **5**. Similarly, the internally threaded member **66** meshes with the second set of external threads **70** so as to lock the working catheter **42** in the stowed position as shown in FIG. **4**.

As further shown in FIG. **8**, a proximal stop **72** is provided to limit proximal movement of the internally threaded member **66** relative to the working catheter **42**. Similarly, a distal stop **74** is provided to limit distal movement of the internally threaded member **66** relative to the working catheter **42**.

While the locking mechanism **56** which is particularly shown in FIGS. **4**, **5**, **6A**, **6B**, **7A**, and **8** as possessing

cooperating internal and external threads, and has substantial benefits, numerous other types of locking mechanisms may be used as the locking mechanism **56** (see FIG. **3**) and still achieve many of the advantages of the present invention.

For example, another locking mechanism which may be used as the locking mechanism **56** (see FIG. **3**) is a detent and groove type locking mechanism (not shown). In particular, such a locking mechanism would include a first groove and a second groove which are (i) spaced apart from each other, and (ii) each defined in an outer surface of the working catheter **42** (the sidewall of the working catheter may need to possess an increased thickness in order to define such grooves therein). A detent (e.g. a ball), supported by the guide catheter **34**, may be spring biased into the first groove so as to lock the working catheter **42** in relation to the guide catheter **34** thereby locking the working catheter **42** in the operative position. When desired, the detent may be allowed to advance out of the first groove and into the second groove. Thereafter, the detent may be spring biased into the second groove so as to lock the working catheter **42** in relation to the guide catheter **34** thereby locking the working catheter **42** in the stowed position. Examples of detent and groove type locking mechanisms which may be used with some modifications as the locking mechanism **56** of the present invention are disclosed in U.S. Pat. Nos. 4,900,202 and 5,013,194 each issued to Wienhold, and U.S. Pat. Nos. 5,470,180 and 5,779,404 each issued to Jore.

Yet another example of a locking mechanism which may be used as the locking mechanism **56** (see FIG. **3**) is a leg and guide channel type locking mechanism (not shown). In particular, such a locking mechanism would include a short leg extending from an outer surface of the working catheter **42**. The leg would be fixed in relation to the working catheter **42**. The locking mechanism would further include a guide channel defined in a sidewall of the guide catheter **34**. The guide channel would extend longitudinally for a short distance (e.g. a few centimeters) along the length of the guide catheter **34**. At the proximal end of the guide channel, there would exist a narrowed proximal channel portion of reduced width. Similarly, at the distal end of the guide channel, there would exist a narrowed distal channel portion of reduced width. In operation, the leg would be positioned in the guide channel. If it would be desirable to lock the working catheter **42** in relation to the guide catheter **34** so as to lock the working catheter **42** in the operative position, the working catheter **42** could be advanced distally in relation to the guide catheter **34** until the leg became wedged within the narrowed distal channel portion. A secondary safety latch may be employed to retain the leg in the narrowed distal channel portion. On the other hand, if it would be desirable to lock the working catheter **42** in relation to the guide catheter **34** so as to lock the working catheter **42** in the stowed position, the working catheter **42** could be advanced proximally in relation to the guide catheter **34** until the leg became wedged within the narrowed proximal channel portion. Similarly, another secondary safety latch may be employed to retain the leg in the narrowed proximal channel portion.

I(a). Placement of the Catheter System **12** Within the Body

The catheter system **12** is placed within the body **14** using the tunneled catheter technique. In particular, a first opening is created by making a small incision in the skin **20** with a scalpel directly over the right internal jugular vein **26**. Thereafter, the right internal jugular vein **26** is punctured to create a venotomy **76** (see FIGS. **9–11**) at a location directly below the first opening by advancing a needle through the skin incision and the subcutaneous tissue **22** and into the right internal jugular vein **26**. Thereafter, a guidewire is advanced through the needle into the right internal jugular vein **26** through the venotomy **76**. The needle is then removed over the guidewire. One or more tubular vessel dilators is passed over the guidewire to widen the opening defined in the skin **20** and subcutaneous tissue **22**, and further to widen the venotomy **76** defined in the wall of the right internal jugular vein **26** to a caliber similar to that of a tubular guide. Thereafter, the tubular guide is advanced over the guidewire and into the right internal jugular vein **26**. Then, a second opening is created in the skin **20** which is spaced apart at least several centimeters from the first opening. A tunneling instrument is advanced from the second opening to the first opening so as to create a passageway within the subcutaneous tissue **22** under the skin **20** between the first opening and the second opening. The catheter system **12** is then advanced into the second opening and through the passageway such that the distal guide orifice **40** of the guide catheter **34** is located adjacent to the first opening. Note that during the above-described advancement of the catheter system **12**, the working catheter **42** is locked to the guide catheter **34** in the stowed position (see e.g. FIG. **4**).

The distal end of the catheter system **12** is then inserted through the tubular guide member and into the right internal jugular vein **26** so that the tissue ingrowth member **43** is positioned in the subcutaneous tissue **22**. Thereafter, the tubular guide member is removed. The first opening is then closed with suture whereby the catheter system **12**: (a) is no longer exposed through the first opening, (b) extends for at least several centimeters under the skin **20** between the second opening and the venotomy **76**, and (c) extends out of the second opening so that the proximal end of the catheter system **12** is located outside of the body **14** as shown in FIG. **10**.

Note that after the catheter system **12** is placed in the vascular system **24** as described above, the catheter system **12** is positioned in the right internal jugular vein **26**, the right innominate vein **30**, and the superior vena cava **32** as shown in FIG. **10**. Moreover, note that as the tissue ingrowth member **43** remains in contact with the subcutaneous tissue **22** over a period of time, the subcutaneous tissue **22** becomes affixed to the tissue ingrowth member **43** thereby securing the catheter system **12** to the body **14**. As discussed above, affixation of the tissue ingrowth member **43** to the subcutaneous tissue **22** in the above described manner helps prevent bacterial migration up the catheter system **12** from the second opening to the venotomy **76** thereby preventing serious infection.

1(b). Performance of a Dialysis Session with the Catheter System **12**

Once the catheter system **12** is placed in the body **14** as described above, the catheter system is positioned as shown in FIG. **10**. In this position, the working catheter **42** is locked in the stowed position. When a patient desires to be dialyzed (i.e. engage in a dialysis session), the egress line **47** and the ingress line **45** are respectively connected to the inlet line **16** and the outlet line **18** of the hemodialysis machine **10** as shown in FIG. **1**.

Thereafter, the working catheter **42** is unlocked from the guide catheter **34** by rotating the internally threaded member **66** so as to unscrew the internally threaded member **66** out of meshing engagement with the second set of external threads **70** which are defined in the exterior surface of the working catheter **42**. The working catheter **42** is then advanced in a distal direction relative to the guide catheter

34 thereby exposing the distal working segment 55 of the working catheter 42 to the blood flow within the superior vena cava 32. Thereafter, the working catheter 42 is locked to the guide catheter 34 in the operative position as shown in FIG. 11. In particular, the internally threaded member 66 is rotated so as to screw the internally threaded member 66 into meshing engagement with the first set of external threads 68 which are defined in the exterior surface of the working catheter 42.

Moving the working catheter 42 from its stowed position (FIG. 10) to its operative position (FIG. 11), causes the first distal working orifice 50 and the second distal working orifice 54 to be exposed to the blood flow within the superior vena cava 32. With the working catheter 42 locked in the operative position, a dialysis procedure is then performed on the patient's body 14 in a well known manner.

Upon completion of the dialysis procedure, the working catheter 42 is unlocked from the guide catheter 34 by rotating the internally threaded member 66 so as to unscrew the internally threaded member 66 out of meshing engagement with the first set of external threads 68. The working catheter 42 is then advanced in a proximal direction relative to the guide catheter 34 thereby withdrawing the distal working segment 55 of the working catheter 42 out of contact with the blood flow in the superior vena cava 32 and into the guide lumen 36 of the guide catheter. Thereafter, the working catheter 42 is locked to the guide catheter 34 in the stowed position thereby assuming the position as shown in FIG. 10. In particular, the internally threaded member 66 is rotated so as to screw the internally threaded member 66 into meshing engagement with the second set of external threads 70.

After the working catheter 42 is locked in its stowed position, the egress line 47 and ingress line 45 are respectively disconnected from the inlet line 16 and the outlet line 18. The proximal orifices 48 and 52 are then each covered with any suitable device (e.g. adapters or injection caps C1, C2), and the patient is able to carry on about his/her business. Thereafter, when a patient desires to be dialyzed again, the above procedure is repeated.

With the catheter system 12 of the present invention, it should be appreciated that the length of time which the distal orifices 50, 54 of the working catheter 42 are exposed to the blood flow in the superior vena cava 32 is substantially reduced relative to the length of time which the corresponding distal orifices of conventional hemodialysis catheters are exposed. This reduction in blood flow exposure time substantially reduces the likelihood that the distal orifices 50, 54 will become partially or totally occluded due to attachment or build-up of blood clots, such as fibrin, on the outer and inner surfaces of the distal working segment 55 of the working catheter 42.

In order to further reduce the likelihood that the distal orifices 50, 54 will become partially or totally occluded due to blood clot attachment or build-up, a quantity of blood clot dissolving liquid may be advanced into the catheter system 12 after a dialysis session is completed in order to flush the fluid flow paths of the working catheter 42 and create a pool in which the distal working segment 55 of the working catheter 42 may be bathed. In particular, after the egress line 47 and ingress line 45 are respectively disconnected from the inlet line 16 and the outlet line 18 following completion of dialysis session, a quantity of blood clot dissolving liquid may be advanced into the egress line 47 and/or the ingress line 45. Advancement of the blood clot dissolving liquid into the egress line 47 causes flushing of the following portions of the working catheter 42: (i) the second proximal working orifice 52, (ii) the egress line 47, (iii) the egress lumen 46, and (iv) the second distal working orifice 54. Similarly, advancement of the blood clot dissolving liquid into the ingress line 45 causes flushing of the following portions of the working catheter 42: (i) the first proximal working orifice 48, (ii) the ingress line 45, (iii) the ingress lumen 44, and (iv) the first distal working orifice 50. Advancement of the blood clot dissolving liquid into the catheter system 12 may be continued until substantially all of the blood is removed from (i) the working catheter 42, and (ii) the guide lumen 36 of the guide catheter 34. This may require an amount of the blood clot dissolving liquid to be advanced past the distal valve 37 and out of the distal orifice 40 of the guide catheter 34. Advancement of the blood clot dissolving liquid into the catheter system 12 in the above-described manner causes an amount of the blood clot dissolving liquid to become trapped or pooled within the guide lumen 36 of the guide catheter 34 at a location which is proximal to the distal valve 37 and distal to the proximal valve 39. While the blood clot dissolving liquid is pooled within the guide lumen 36 of the guide catheter 34 at the above-described location, the blood clot dissolving liquid contacts the working catheter 42 at the first distal working opening 50 and the second distal working opening 54. This advantageously helps prevent total or even partial occlusion of the orifices 50, 54 due to blood clot build-up. One type of blood clot dissolving liquid which may be used with the present invention is urokinase.

After the blood clot dissolving liquid is advanced into the catheter system 12 in the above-described manner, then the proximal orifices 48 and 52 are each sealed with any suitable device (e.g. adapters or injection caps C1, C2), and subsequently the patient is able to carry on about his/her business. The above flushing procedure may be repeated after each dialysis session is completed.

While advancement of the blood clot dissolving liquid (such as urokinase) into the guide lumen 36 of the guide catheter 34 after a dialysis session has been completed has many advantages, some advantages may also be achieved by advancement of an alternative solution into the catheter system 12 after a dialysis session. For example, instead of advancing blood clot dissolving liquid (such as urokinase) into the catheter system 12 after a dialysis session, a heparin lock flush solution may be advanced into the catheter system 12 after a dialysis session has been completed in order to flush the fluid flow paths of the working catheter 42 and create a pool in which the distal working segment 55 of the working catheter 42 may be bathed.

It should be noted that while the distal valve 37 helps maintain the flushing solution (e.g. urokinase or heparin) within the guide lumen 36 of the guide catheter 34 of the catheter system 12 during idle periods when the working catheter is positioned in the stowed position, the distal valve 37 also helps prevent blood which is flowing in the superior vena cava flow from advancing into contact with the distal orifices 50, 54 of the working catheter 42 of the catheter system 12 during idle periods when the working catheter is positioned in the stowed position.

It should further be understood that the distal valve 37 and the proximal valve 39 help prevent blood from escaping through the catheter system 12 during idle periods (i.e. after completion of a dialysis session and before commencement of a subsequent dialysis session). It should also be appreciated that during a dialysis session, the valves 37 and 39 function to prevent blood and/or air leakage through a space defined between the outer surface of the working catheter 42 and the inner surface of the guide catheter 34.

Please note that the working catheter **42** of the catheter system **12** contacts the blood located in the vascular system **24** for a substantially reduced amount of time (i.e. only while the patient is undergoing dialysis) in comparison to the amount of time a conventional dialysis catheter is being contacted by blood located in the vascular system (i.e. at all times). Accordingly, the physical structure of the working catheter **42** may be substantially the same or similar to the physical structure of a conventional short-term catheter. For example, the thickness of the sidewalls of the working catheter **42** which define the ingress lumen **44** and the egress lumen **46** may be made to be substantially thinner than the thickness of the sidewalls which define the corresponding lumens of a conventional long-term dialysis catheter. This may help reduce the necessary magnitude of the outer diameter of the guide catheter **34** in which the working catheter **42** is positionable.

II. Catheter System **200**

FIGS. **12–13** show a catheter system **200** which also incorporates the features of the present invention therein. The catheter system **200** is somewhat similar to the catheter system **12**. Thus, the same reference numerals are used in FIGS. **12–13** to designate common components which were previously discussed with regard to FIGS. **1–11**. Moreover, the description of the components of the catheter system **200** which are common to the catheter system **12** will not be undertaken since they are designated with common reference numerals and such components have been previously described hereinabove. In addition, the catheter system **200** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). Furthermore, the catheter system **200** is used to perform a dialysis procedure in substantially the same manner as was described hereinabove with respect to the performance of a dialysis procedure with the catheter system **12** (see e.g. Section 1(b) entitled: "Performance of a Dialysis Session with the Catheter System **12**").

However, the catheter system **200** differs from the catheter system **12** in that a portion of the distal working segment **55** of the working catheter **42** which extends out of the distal guide orifice **40** of the guide catheter **34** when the working catheter **42** is locked in the operative position is arranged in a bifurcated configuration as shown in FIG. **12**. In particular, a distal portion of the ingress lumen **44** (near the first distal working orifice **50**) is arranged so as to gradually extend away from a distal portion of the egress lumen **46** (near the second distal working orifice **54**) as shown in FIG. **12**.

The working catheter **42**, shown in FIGS. **12–13**, possesses a distal portion configured somewhat similar to the distal portion of a dialysis catheter disclosed in an article entitled "Management of Hemodialysis Catheters" which was published in the July, 1999 edition of the periodical entitled "Applied Radiology" at pages 14–24 (authored by Haskel et al.), the disclosure of which is hereby incorporated by reference. Catheters having a distal portion configured in the above-described manner are sometimes referred to in the relevant medical art as "split-tip" catheters. For example, on page 20 of the Haskel article, a "split-tip" catheter is shown in FIG. **8**.

The locking mechanism **56** functions to lock the working catheter **42** to the guide catheter **34** in either the stowed position (FIG. **13**) or the operative position (FIG. **12**). It should be appreciated that FIG. **13** shows the working catheter **42** locked to the guide catheter **34** in the stowed position. While the working catheter **42** is locked in the stowed position in the patient's body **14** between dialysis sessions, the distal orifices **50, 54** of the working catheter **42** are isolated from contact with the blood flow in the superior vena cava **32**. FIG. **12** shows the working catheter **42** locked to the guide catheter **34** in the operative position. While the working catheter **42** is locked in the operative position during performance of a dialysis procedure, the distal orifices **50, 54** of the working catheter **42** are positioned within the blood flow in the superior vena cava **32**.

Also, please note that the working catheter **42** of the catheter system **200** contacts the blood located in the vascular system **24** for a substantially reduced amount of time in comparison to the amount of time a conventional dialysis catheter is being contacted by blood located in the vascular system. Accordingly, the physical structure of the working catheter **42** of the catheter system **200** may be substantially the same or similar to the physical structure of a conventional short-term catheter for the same reasons hereinabove discussed in regard to the dialysis catheter **42** of the catheter system **12** in section 1(b) entitled "Performance of a Dialysis Session with the Catheter System **12**".

III. Catheter System **300**

FIGS. **14–15** show a catheter system **300** which also incorporates the features of the present invention therein. The catheter system **300** includes a guide catheter **302**, a first single lumen working catheter **303**, and a second single lumen working catheter **304**. The catheter system **300** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). Furthermore, the catheter system **300** is used to perform a dialysis procedure in substantially the same manner as was described hereinabove with respect to the performance of a dialysis procedure with the catheter system **12** (see e.g. Section 1 (b) entitled: "Performance of a Dialysis Session with the Catheter System **12**").

The guide catheter **302** has a first guide lumen **308** and a second guide lumen **310** each which extends along the length of the guide catheter **302** as shown in FIG. **14**. The first guide lumen **308** defines a first distal guide orifice **314**, while the second guide lumen **310** defines a second distal guide orifice **318** (see FIG. **15**). The first working catheter **303** is positioned within the guide lumen **308** of the guide catheter **302**, while the second working catheter **304** is positioned within the guide lumen **310** of the guide catheter **302** as shown in FIGS. **14–15**.

The guide catheter **302** has a tissue ingrowth member **320** secured to an outer surface thereof. The tissue ingrowth member **320** is substantially identical to tissue ingrowth member **43** described hereinabove with regard to the catheter system **12**.

The first working catheter **303** includes a lumen **334**. The lumen **334** defines a distal orifice **336**. Similarly, the second working catheter **304** includes a lumen **338**. The lumen **338** defines a distal orifice **340**. The distal orifice **336** is defined in a distal segment **342** of the first working catheter **303**. Similarly, the distal orifice **340** is defined in a distal segment **344** of the second working catheter **304**.

The catheter system **300** additionally includes a first locking mechanism **321** and a second locking mechanism **323** each which is schematically shown in FIG. **14**. Each of the locking mechanisms **321, 323** is substantially identical to the locking mechanism **56** described hereinabove with regard to the catheter system **12**. In particular, the first locking mechanism **321** operates to lock the first working catheter **303** in relation to the guide catheter **302** at any one of two positions, while the second locking mechanism **323**

also operates to lock the second working catheter **304** in relation to the guide catheter **302** at any one of two positions. In particular, the first locking mechanism **321** may lock the first working catheter **303** relative to the guide catheter **302** in an operative position (see FIG. **14**) or in a stowed position (see FIG. **15**). Similarly, the second locking mechanism **323** may lock the second working catheter **304** relative to the guide catheter **302** in an operative position (see FIG. **14**) or in a stowed position (see FIG. **15**).

It should be noted that when the first working catheter **303** is locked in the operative position, (i) the first working catheter **303** extends through the first guide lumen **308** of the guide catheter **302** and out of the first distal guide orifice **314** of the guide catheter **302**, and (ii) the distal orifice **336** is positioned outside of the guide catheter **302**. On the other hand, when the first working catheter **303** is locked in the stowed position, (i) the first working catheter **303** extends into the first guide lumen **308** of the guide catheter **302**, and (ii) the distal orifice **336** is positioned within the first guide lumen **308** of the guide catheter **302**.

Similarly, when the second working catheter **304** is locked in the operative position, (i) the second working catheter **304** extends through the second guide lumen **310** of the guide catheter **302** and out of the second distal guide orifice **318** of the guide catheter **302**, and (ii) the distal orifice **340** is positioned outside of the guide catheter **302**. On the other hand, when the second working catheter **304** is locked in the stowed position, (i) the second working catheter **304** extends into the second guide lumen **310** of the guide catheter **302**, and (ii) the distal orifice **340** is positioned within the second guide lumen **310** of the guide catheter **302**.

The guide catheter **302** further includes a pair of distal blood flow valves **330** and a pair of proximal blood flow valves **332** positioned within the guide lumens **308, 310** as shown in FIGS. **14–15**. The blood flow valves **330** and **332** are substantially identical to the blood flow valves **37** and **39** which were described hereinabove with regard to the catheter system **12**.

A clamp **346** is positioned on the first working catheter **303**, while another clamp **348** is positioned on the second working catheter **304**. The clamps **346, 348** are substantially identical in construction and function to the clamps **62, 64** discussed hereinabove with regard to the catheter system **12**.

The catheter system **300** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). While in the body **14**, the locking mechanism **321** functions to lock the first working catheter **303** to the guide catheter **302** in either its stowed position (FIG. **15**) or its operative position (FIG. **14**). Similarly, while in the body **14**, the locking mechanism **323** functions to lock the second working catheter **304** to the guide catheter **302** in either its stowed position (FIG. **15**) or its operative position (FIG. **14**).

It should be appreciated that FIG. **15** shows the first working catheter **303** locked to the guide catheter **302** in the stowed position. While the first working catheter **303** is locked in the stowed position in the patient's body **14** between dialysis sessions, the distal orifice **336** of the first working catheter **303** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **14** shows the first working catheter **303** locked to the guide catheter **302** in the operative position. While the first working catheter **303** is locked in the operative position in the patient's body **14** during performance of a dialysis procedure, the distal orifice **336** of the first working catheter **303** would be positioned within the blood flow in the superior vena cava **32**.

Similarly, FIG. **15** shows the second working catheter **304** locked to the guide catheter **302** in the stowed position. While the second working catheter **304** is locked in the stowed position in the patient's body **14** between dialysis sessions, the distal orifice **340** of the second working catheter **304** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **14** shows the second working catheter **304** locked to the guide catheter **302** in the operative position. While the second working catheter **304** is locked in the operative position in the patient's body **14** during performance of a dialysis procedure, the distal orifice **340** of the second working catheter **304** would be positioned within the blood flow in the superior vena cava **32**.

Also, please note that the working catheters **303, 304** of the catheter system **300** contact the blood located in the vascular system **24** for a substantially reduced amount of time in comparison to the amount of time a conventional dialysis catheter is being contacted by blood located in the vascular system. Accordingly, the physical structure of the working catheters **303, 304** of the catheter system **300** may be substantially the same or similar to the physical structure of a conventional short-term catheter for the same reasons hereinabove discussed in regard to the dialysis catheter **42** of the catheter system **12** in section 1(b) entitled "Performance of a Dialysis Session with the Catheter System **12**".

The catheter system **300** is shown in FIGS. **14** and **15** as having the distal segment of the guide lumen **310**located adjacent to the guide lumen **308**. In the embodiment shown in FIGS. **14** and **15**, the guide catheter **302** can be said to possess a side-by-side configuration. An alternative to providing the guide catheter **302** with a side-by-side configuration is shown in FIG. **16**. In particular, a distal portion of the guide lumens **308, 310** of the catheter system **300** may be alternatively configured so that the distal portion of the guide catheter **302** is arranged in a bifurcated configuration as shown in FIG. **16**. In such a configuration, the distal portion of the guide lumen **310** is arranged so as to gradually extend away from the distal portion of the guide lumen **308** as shown in FIG. **16**. In the embodiment shown in FIG. **16**, the guide catheter **302** can be said to possess a "split-tip" configuration.

IV. Catheter System **400**

FIGS. **17–18** show a catheter system **400** which also incorporates the features of the present invention therein. The catheter system **400** includes a guide catheter **402** and a single lumen working catheter **404**. The guide catheter **402** has an active lumen **408** and a guide lumen **410** each which extends along the length of the guide catheter **402** as shown in FIG. **17**. The guide lumen **410** defines a distal guide orifice **414**. The working catheter **404** is positioned within the guide lumen **410** of the guide catheter **402**.

The catheter system **400** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). Furthermore, the catheter system **400** is used to perform a dialysis procedure in substantially the same manner as was described hereinabove with respect to the performance of a dialysis procedure with the catheter system,**12** (see e.g. Section 1 (b) entitled: "Performance of a Dialysis Session with the Catheter System **12**").

The guide catheter **402** has a tissue ingrowth member **416** secured to an outer surface thereof. The tissue ingrowth member **416** is substantially identical to tissue ingrowth member **43** described hereinabove with regard to the catheter system **12**.

The working catheter **404** defines a lumen **405** through which fluid, such as blood, may be advanced. The lumen **405**

defines a distal orifice **426**. The distal orifice **426** is defined in a distal segment **428** of the working catheter **404**.

The catheter system **400** additionally includes a locking mechanism **421** which is schematically shown in FIG. **17**. The locking mechanism **421** is substantially identical to the locking mechanism **56** described hereinabove with regard to the catheter system **12**. In particular, the locking mechanism **421** operates to lock the working catheter **404** in relation to the guide catheter **402** at any one of two positions. In particular, the locking mechanism **421** may lock the working catheter **404** relative to the guide catheter **402** in an operative position (see FIG. **17**) or in a stowed position (see FIG. **18**).

It should be noted that when the working catheter **404** is locked in the operative position, (i) the working catheter **404** extends through the guide lumen **410** of the guide catheter **402** and out of the distal guide orifice **414** of the guide catheter **402**, and (ii) the distal orifice **426** of the working catheter **404** is positioned outside of the guide catheter **402**. On the other hand, when the working catheter **404** is locked in the stowed position, (i) the working catheter **404** extends into the guide lumen **410** of the guide catheter **402**, and (ii) the distal orifice **426** is positioned within the guide lumen **410** of the guide catheter **402**.

The guide catheter **402** further includes a distal blood flow valve **422** and a proximal blood flow valve **424** positioned within the guide lumen **410** as shown in FIGS. **17** and **18**. The blood flow valves **422** and **424** are substantially identical to the blood flow valves **37** and **39** which were described hereinabove with regard to the catheter system **12**. The guide catheter **402** may further include an additional distal blood flow valve (not shown) located in the distal portion of the active lumen **408** and an additional proximal blood flow valve (not shown) located in the proximal portion of the active lumen **408**. These additional blood flow valves would also be substantially identical to the blood flow valves **37** and **39** which were described hereinabove with regard to the catheter system **12**.

A clamp **430** is positioned on the working catheter **404**. Another clamp **431** is positioned on the guide catheter **402** as shown in FIG. **17**. The clamps **430**, **431** are substantially identical in construction and function to the clamps **62**, **64** discussed hereinabove with regard to the catheter system **12**.

The catheter system **400** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). While in the body **14**, the locking mechanism **421** functions to lock the working catheter **404** to the guide catheter **402** in either its stowed position (FIG. **18**) or its operative position (FIG. **17**).

It should be appreciated that FIG. **18** shows the working catheter **404** locked to the guide catheter **402** in the stowed position. While the working catheter **404** is locked in the stowed position in the patient's body **14** between dialysis sessions, the distal orifice **426** of the working catheter **404** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **17** shows the working catheter **404** locked to the guide catheter **402** in the operative position. While the working catheter **404** is locked in the operative position during performance of a dialysis procedure, the distal orifice **426** of the working catheter **404** would be positioned within the blood flow in the superior vena cava **32**.

Also, please note that the working catheter **404** of the catheter system **400** contacts the blood located in the vascular system **24** for a substantially reduced amount of time in comparison to the amount of time a conventional dialysis catheter is being contacted by blood located in the vascular system. Accordingly, the physical structure of the working catheter **404** of the catheter system **400** may be substantially the same or similar to the physical structure of a conventional short-term catheter for the same reasons hereinabove discussed in regard to the dialysis catheter **42** of the catheter system **12** in section 1 (b) entitled "Performance of a Dialysis Session with the Catheter System **12**".

The catheter system **400** is shown in FIGS. **17** and **18** as having the distal segment of the guide lumen **410** located adjacent to the active lumen **408**. In the embodiment shown in FIGS. **17** and **18**, the guide catheter **402** can be said to possess a side-by-side configuration. An alternative to providing the guide catheter **402** with a side-by-side configuration is shown in FIGS. **19**. In particular, a distal portion of both the guide lumen **410** and the active lumen **408** of the catheter system **400** may be alternatively configured so that the distal portion of the guide catheter **402** is arranged in a bifurcated configuration as shown in FIG. **19**. In such a configuration, the distal portion of the guide lumen **410** is arranged so as to gradually extend away from the distal portion of the active lumen **408** as shown in FIG. **19**. In the embodiment shown in FIG. **19**, the guide catheter **402** can be said to possess a "split-tip" configuration.

In addition, the catheter system **400** is shown in FIGS. **17** and **18** as having the working catheter **404** positioned within the guide lumen **410** of the guide catheter **402** while the active lumen **408** does not receive any such catheter therein. In an alternative embodiment of the present invention which is shown in FIG. **20**, the catheter system **400** may be modified such that the working catheter **404** would be positioned within the lumen **408** of the guide catheter **402**, while the lumen **410** would not receive any such catheter therein. In such an embodiment, the lumen **410** would function as an active lumen through which a fluid, such as blood, may be advanced therethrough. Further, in such an embodiment, the lumen **408** would function as a guide lumen.

V. Catheter System **500**

FIGS. **21–23** show a catheter system **500** which further incorporates the features of the present invention therein. The catheter system **500** includes a first catheter apparatus **501** and a second catheter apparatus **503**. The first catheter apparatus **501** includes a first guide catheter **502** and a first single lumen working catheter **506**, while the second catheter apparatus **503** includes a second guide catheter **504** and a second single lumen working catheter **508**.

The catheter system **500** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. each catheter apparatus **501**, **503** is placed within the body by the tunneled catheter technique). Furthermore, the catheter system **500** is used to perform a dialysis procedure in substantially the same manner as was described hereinabove with respect to the performance of a dialysis procedure with the catheter system **12** (see e.g. Section 1(b) entitled: "Performance of a Dialysis Session with the Catheter System **12**").

The first guide catheter **502** has a first guide lumen **514** defined therein which extends along the length of the guide catheter **502** as shown in FIG. **21**. The second guide catheter **504** has a second guide lumen **516** defined therein which extends along the length of the guide catheter **504** as also shown in FIG. **21**. The first guide lumen **514** defines a first distal guide orifice **520**, while the second guide lumen **516** defines a second distal guide orifice **524**.

The first working catheter **506** is positioned within the guide lumen **514** of the guide catheter **502**, while the second

working catheter **508** is positioned within the guide lumen **516** of the guide catheter **504** as shown in FIGS. **21–22**.

Referring to FIGS. **21** and **23**, the first guide catheter **502** has a tissue ingrowth member **530** secured to an outer surface thereof, while the second guide catheter **504** has a tissue ingrowth member **532** secured to an outer surface thereof. The tissue ingrowth members **530, 532** are substantially identical to tissue ingrowth member **43** described hereinabove with regard to the catheter system **12**.

The first working catheter **506** includes a lumen **550**. The lumen **550** defines a distal orifice **552**. Similarly, the second working catheter **508** includes a lumen **554**. The lumen **554** defines a distal orifice **556**. The distal orifice **552** is defined in a distal segment **558** of the first working catheter **506**. Similarly, the distal orifice **556** is defined in a distal segment **560** of the second working catheter **508**.

The catheter system **500** additionally includes a first locking mechanism **521** and a second locking mechanism **523** each which is schematically shown in FIGS. **21** and **23**. Each of the locking mechanisms **521, 523** is substantially identical to the locking mechanism **56** described hereinabove with regard to the catheter system **12**. In particular, the first locking mechanism **521** operates to lock the first working catheter **506** in relation to the first guide catheter **502** at any one of two positions, while the second locking mechanism **523** also operates to lock the second working catheter **508** in relation to the second guide catheter **504** at any one of two positions. In particular, the first locking mechanism **521** may lock the first working catheter **506** relative to the first guide catheter **502** in an operative position (see FIG. **21**) or in a stowed position (see FIG. **22**). Similarly, the second locking mechanism **523** may lock the second working catheter **508** relative to the second guide catheter **504** in an operative position (see FIG. **21**) or in a stowed position (see FIG. **22**).

It should be noted that when the first working catheter **506** is locked in the operative position, (i) the first working catheter **506** extends through the first guide lumen **514** of the first guide catheter **502** and out of the first distal guide orifice **520** of the first guide catheter **502**, and (ii) the distal orifice **552** of the first working catheter **506** is positioned outside of the first guide catheter **502**. On the other hand, when the first working catheter **506** is locked in the stowed position, (i) the first working catheter **506** extends into the first guide lumen **514** of the first guide catheter **502**, and (ii) the distal orifice **552** of the first working catheter **506** is positioned within the first guide lumen **514** of the first guide catheter **502**.

Similarly, when the second working catheter **508** is locked in the operative position, (i) the second working catheter **508** extends through the second guide lumen **516** of the second guide catheter **504** and out of the second distal guide orifice **524** of the second guide catheter **504**, and (ii) the distal orifice **556** of the second working catheter **508** is positioned outside of the second guide catheter **504**. On the other hand, when the second working catheter **508** is locked in the stowed position, (i) the second working catheter **508** extends into the second guide lumen **516** of the second guide catheter **504**, and (ii) the distal orifice **556** of the second working catheter **508** is positioned within the second guide lumen **516** of the second guide catheter **504**.

The first guide catheter **502** further includes a distal blood flow valve **542** and a proximal blood flow valve **544** positioned within the first guide lumen **514** as shown in FIGS. **21** and **22**. The second guide catheter **504** further includes a distal blood flow valve **546** and a proximal blood flow valve **548** positioned within the second guide lumen **516** as also shown in FIGS. **21** and **22**. The blood flow valves **542, 544, 546,** and **548** are substantially identical to the blood flow valves **37** and **39** which were described hereinabove with regard to the catheter system **12**.

A clamp **562** is positioned on the first working catheter **506**, while another clamp **564** is positioned on the second working catheter **508**. The clamps **562, 564** are substantially identical in construction and function to the clamps **62, 64** discussed hereinabove with regard to the catheter system **12**.

The catheter system **500** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. both catheter apparatus **501** and **503** are placed in the body **14** using the tunneled catheter technique). While in the body **14**, the locking mechanism **521** functions to lock the first working catheter **506** to the first guide catheter **502** in either its stowed position (FIG. **22**) or its operative position (FIG. **21**). Similarly, while in the body **14**, the locking mechanism **523** functions to lock the second working catheter **508** to the second guide catheter **504** in either its stowed position (FIG. **22**) or its operative position (FIG. **21**).

It should be appreciated that FIG. **22** shows the first working catheter **506** locked to the first guide catheter **502** in the stowed position. While the first working catheter **506** is locked in the stowed position in the patient's body **14** between dialysis sessions, the distal orifice **552** of the first working catheter **506** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **21** shows the first working catheter **506** locked to the first guide catheter **502** in the operative position. While the first working catheter **506** is locked in the operative position during performance of a dialysis procedure, the distal orifice **552** of the first working catheter **506** would be positioned within the blood flow in the superior vena cava **32**.

Also, please note that the working catheters **506, 508** of the catheter system **500** contact the blood located in the vascular system **24** for a substantially reduced amount of time in comparison to the amount of time a conventional dialysis catheter is being contacted by blood located in the vascular system. Accordingly, the physical structure of the working catheters **506, 508** of the catheter system **500** may be substantially the same or similar to the physical structure of a conventional short-term catheter for the same reasons hereinabove discussed in regard to the dialysis catheter **42** of the catheter system **12** in section 1(b) entitled "Performance of a Dialysis Session with the Catheter System **12**".

Similarly, FIG. **22** shows the second working catheter **508** locked to the second guide catheter **504** in the stowed position. While the second working catheter **508** is locked in the stowed position in the patient's body **14** between dialysis sessions, the distal orifice **556** of the second working catheter **508** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **21** shows the second working catheter **508** locked to the second guide catheter **504** in the operative position. While the second working catheter **508** is locked in the operative position during performance of a dialysis procedure, the distal orifice **556** of the second working catheter **508** would be positioned within the blood flow in the superior vena cava **32**.

The catheter system **500** is shown in FIGS. **21–23** as having the ability to retract and lock (i) the first working catheter **506** of the first catheter apparatus **501** in relation to the first guide catheter **502**, as well as (ii) the second working catheter **508** of the second catheter apparatus **503** in relation to the second guide catheter **504**. However, it should be appreciated that a first alternative arrangement (not shown) to the arrangement described in FIGS. **21–23** is to

configure the second catheter apparatus **503** to be exactly the same as shown in FIGS. **21–23**, but to configure the first catheter apparatus **501** to be similar to a conventional single lumen catheter (i.e. a catheter apparatus which does not possess a retractable inner working catheter). It should be further appreciated that a second alternative arrangement (not shown) to the arrangement described in FIGS. **21–23** is to configure the first catheter apparatus **501** to be exactly the same as shown in FIGS. **21–23**, but to configure the second catheter apparatus **503** to be similar to a conventional single lumen catheter (i.e. a catheter apparatus which does not possess a retractable inner working catheter).

VI. Catheter System **600**

FIGS. **24–26** show a catheter system **600** which additionally incorporates the features of the present invention therein. The catheter system **600** may be used for the administration of total parenteral nutrition (hereinafter referred to as "TPN") to a patient. TPN generally refers to intravenous feeding via an indwelling central venous catheter of nutritive material in conditions where patients cannot eat by mouth or receive nutrition enterally (e.g. by gastric tube or small bowel tube). Some examples where prolonged administration of TPN to a patient are indicated include instances where a patient suffers from an insufficient small bowel absorptive area such as short gut syndrome or an instance where a patient suffers from prolonged intestinal ileus which may have resulted due to a severe burn injury or an abdominal surgery. Other examples where prolonged administration of TPN to a patient are indicated include instances where a patient has a condition requiring prolonged bowel rest such as where the patient suffers from pancreatitis or inflammatory bowel disease. Yet another example where prolonged administration of TPN to a patient is indicated is the situation where a patient refuses to eat such as would occur in the case of severe anorexia nervosa.

Referring now in detail to FIGS. **24–26**, the catheter system **600** includes a guide catheter **602** and a single lumen working catheter **606**. The guide catheter **602** has a guide lumen **614** which extends along the length of the guide catheter **602** as shown in FIG. **24**. The guide lumen **614** defines a distal guide orifice **620**. The working catheter **606** is positioned within the guide lumen **614** of the guide catheter **602** as shown in FIGS. **24–26**.

The catheter system **600** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). Furthermore, the catheter system **600** is used to perform a TPN administration procedure in substantially the same manner as was described hereinabove with respect to the performance of a dialysis procedure with the catheter system **12** (see e.g. Section 1(b) entitled: "Performance of a Dialysis Session with the Catheter System **12**"). In particular, when a patient desires to engage in a TPN administration session, the working catheter **606** is connected to a source of TPN. Thereafter, the working catheter **606** is unlocked from the guide catheter **602**. Then, the working catheter **606** is advanced to its operative position. Once in its operative position, the working catheter **606** is locked to the guide catheter **602** so that a distal segment **658** of the working catheter **606** extends out of the distal guide orifice **620** as shown in FIG. **24**. Thereafter, the TPN administration session is performed in a conventional manner as is well known in the art. Once the TPN administration session is completed, the working catheter **606** is unlocked from the guide catheter **602** and retracted to its stowed position. Once in its stowed position, the working catheter **606** is locked to the guide catheter **602**. Then, the working catheter **606** is disconnected from the source of TPN. Thereafter, the patient is able to carry on about his/her business.

The working catheter **606** includes a lumen **650**. The lumen **650** defines a distal orifice **652**. The distal orifice **652** is defined in the distal segment **658** of the working catheter **606**.

Referring to FIGS. **24** and **26**, the guide catheter **602** has a tissue ingrowth member **630** secured to an outer surface thereof. The tissue ingrowth member **630** is substantially identical to tissue ingrowth member **43** described hereinabove with regard to the catheter system **12**.

The catheter system **600** additionally includes a locking mechanism **621** which is schematically shown in FIGS. **24** and **26**. The locking mechanism **621** is substantially identical to the locking mechanism **56** described hereinabove with regard to the catheter system **12**. In particular, the locking mechanism **621** operates to lock the working catheter **606** in relation to the guide catheter **602** at any one of two positions. In particular, the locking mechanism **621** may lock the working catheter **606** relative to the guide catheter **602** in an operative position (see FIG. **24**) or in a stowed position (see FIG. **25**).

It should be noted that when the working catheter **606** is locked in the operative position, (i) the working catheter **606** extends through the guide lumen **614** of the guide catheter **602** and out of the distal guide orifice **620** of the guide catheter **602**, and (ii) the distal orifice **652** of the working catheter **606** is positioned outside of the guide catheter **602**. On the other hand, when the working catheter **606** is locked in the stowed position, (i) the working catheter **606** extends into the guide lumen **614** of the guide catheter **602**, and (ii) the distal orifice **652** of the working catheter **606** is positioned within the guide lumen **614** of the guide catheter **602**.

The guide catheter **602** further includes a distal blood flow valve **642** and a proximal blood flow valve **644** positioned within the guide lumen **614** as shown in FIGS. **24** and **25**. The blood flow valves **642**, **644** are substantially identical to the blood flow valves **37** and **39** which were described hereinabove with regard to the catheter system **12**.

A clamp **662** is positioned on the working catheter **606**. The clamp **662** is substantially identical in construction and function to the clamps **62**, **64** discussed hereinabove with regard to the catheter system **12**.

The catheter system **600** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). While in the body **14**, the locking mechanism **621** functions to lock the working catheter **606** to the guide catheter **602** in either its stowed position (FIG. **25**) or its operative position (FIG. **24**).

It should be appreciated that FIG. **25** shows the working catheter **606** locked to the guide catheter **602** in the stowed position. While the working catheter **606** is locked in the stowed position in the patient's body **14** between TPN administration sessions, the distal orifice **652** of the working catheter **606** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **24** shows the working catheter **606** locked to the guide catheter **602** in the operative position. While the working catheter **606** is locked in the operative position during performance of a TPN administration procedure, the distal orifice **652** of the catheter **600** would be positioned within the blood flow in the superior vena cava **32**.

Also, please note that the working catheter **606** of the catheter system **600** contacts the blood located in the vas-

cular system **24** for a substantially reduced amount of time in comparison to the amount of time a conventional dialysis catheter is being contacted by blood located in the vascular system. Accordingly, the physical structure of the working catheter **606** of the catheter system **600** may be substantially the same or similar to the physical structure of a conventional short-term catheter for the same reasons hereinabove discussed in regard to the dialysis catheter **42** of the catheter system **12** in section 1(b) entitled "Performance of a Dialysis Session with the Catheter System **12**".

An alternative configuration for the catheter system **600** is shown in FIG. **27**. In particular, this alternative embodiment of the present invention shows a catheter system **600'**. The catheter system **600'** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (i.e. by the tunneled catheter technique). Further, the catheter system **600'** is used in substantially the same manner as herein described with respect to the catheter system **600**. Moreover, the catheter system **600'** is exactly the same in construction and configuration as the catheter system **600** shown in FIGS. **24–26**, with the exception that the catheter system **600'** includes a sideport **670** through which fluid may be withdrawn or otherwise advanced. In particular, the sideport **670** includes a conduit **672** having a set of external threads **674** defined on a proximal end thereof. A clamp **676** is positioned on the conduit **672**. The clamp **662** is substantially identical in construction and function to the clamps **62, 64** discussed hereinabove with regard to the catheter system **12**. The conduit **672** defines a sideport lumen **673** which is in fluid communication with the guide lumen **614**. Accordingly, air can be aspirated out of the guide lumen **614** through the sideport **670** via the conduit **672**. Alternatively, the guide lumen **614** may be flushed with a fluid such as a saline, heparin, or urokinase solution between uses of the catheter system **600'**(e.g. administration of TPN to a patient) while the working catheter **606** is locked in its stowed position (see e.g. FIG. **25**). The guide lumen **614** may also be flushed with a saline, heparin, or urokinase solution while the working catheter **606** is locked in its operative position (see e.g. FIG. **27**).

When not in use, the sideport **670** may be clamped shut with the clamp **676**. Moreover, when not in use, a closure member or cap **678** may be secured to the conduit **672** to cover a proximal sideport orifice **680** which is defined by the conduit **672**. The cap **678** is provided with a set of internal threads which cooperate with the set of external threads **674** so as to lock the cap **678** to the guide catheter **602**. Optionally, the cap **678** may be provided with a silicone membrane **679**, as shown in FIGS. **28–29**, which may be traversed with a needle whereby a saline, heparin, or urokinase solution may be advanced into the conduit **672** in order to flush the guide catheter **602**.

Additionally, while the closure member **678** is disclosed as being locked to the sideport **670** by an arrangement which includes cooperating internal and external threads and has advantages thereby, such closure member **678** may be locked to the sideport **670** by other locking arrangements such as a conventional tamper-proof (or child-proof) arrangement typically used on pill containers that contain prescription medication which is dispensed by a pharmacy.

It should be noted that any of the other embodiments of the present invention set forth herein (e.g. catheter systems **12, 200, 300, 400,** and **500**) may be modified to incorporate a sideport which is similar to sideport **670**. In particular, any of the guide catheters of the catheter systems **12, 200, 300, 400,** and **500** may be modified to include a sideport which is similar in construction, configuration, and use to the construction, configuration and use of the sideport **670** described herein.

VII. Conclusion

While the invention has been illustrated and described in detail in the drawings and foregoing description, the same is to be considered as illustrative and not restrictive in character, it being understood that only the preferred embodiments have been shown and described and that all changes and modifications that come within the spirit of the invention are desired to be protected.

For instance, while the above-described dual-lumen catheter systems (e.g. catheter system **12, 200, 300, 400,** and **500**) were discussed as being effective to perform hemodialysis, such catheter systems can also be utilized to perform other medical procedures in which dual-lumen catheter access to the vascular system (e.g. the central venous system) is required. One example of such a medical procedure is plasmapheresis in which blood is withdrawn from the vascular system, components of the blood are separated outside of the body, and a portion of the blood components are then returned to the vascular system.

In addition, another medical procedure which may be performed using the above-described dual-lumen catheter systems is peritoneal dialysis. In particular, catheter system occlusion may be prevented during a peritoneal dialysis procedure in a manner similar to that described above with respect to the catheter systems **12, 200, 300, 400,** and **500**.

Moreover, while the above-described single-lumen catheter systems (e.g. catheter system **600, 600'**) were discussed as being effective to perform administration of total parenteral nutrition, such catheter systems can be utilized to perform other medical procedures in which single-lumen catheter access to the vascular system is required. Examples of other medical procedures in which single-lumen catheter access to the vascular system is required includes (i) chemotherapy or other long-term medicinal infusions, (ii) repetitive blood transfusions, and (iii) repetitive blood samplings.

Furthermore, each of the above-described catheter systems (e.g. catheter systems **12, 200, 300, 400, 500, 600, 600'**) were described as having a tissue ingrowth member (e.g. tissue ingrowth members **43, 320, 416, 530, 630**) which is configured to facilitate attachment of such catheter system to the subcutaneous tissue **22** of the body. While the provision of such a tissue ingrowth member to effect attachment of such catheter system to the body of a patient has many advantages, the present invention may utilize other mechanisms which can function to attach such catheter system to the body on a long-term or even a short-term basis and still benefit from various advantages of the other features of the present invention. An example of such an attachment mechanism is a plastic member having a hole or recess for receiving a catheter therein and further having one or more wing-like or flap-like extensions which may be sutured or taped to the skin of the patient **14**. Additionally, it is possible that the above-described catheters systems of the present invention (e.g. catheter systems **12, 200, 300, 400, 500, 600, 600'**) may not include any mechanism which specifically functions to attach the catheter systems to the body yet still benefit from some of the advantages of the other features of the present invention.

While the above-described catheter systems **12, 200, 300, 400, 500, 600,** and **600'** were described as being placed in the body **14** utilizing the permanent catheterization technique and has many advantages thereby, such catheter systems **12, 200, 300, 400, 500, 600,** and **600'** could be

placed in the body **14** utilizing other techniques (e.g. the temporary catheterization technique) and still achieve some of the advantages of the present invention.

While the separating diaphragm **39**A is described as being substituted for the proximal valve **39** of the catheter system **12** (see FIG. **8**A), another separating diaphragm, similar to the separating diaphragm **39**A, may also be substituted for the distal valve **37** of the catheter system **12**. Alternatively, the separating diaphragm **39**A may be used in addition to the proximal valve **39** and the distal valve **37** to further prevent blood flow (or air flow) leakage between the guide catheter **34** and the working catheter **42**. Moreover, while the separating diaphragm **39**A is described as alternatively being incorporated into the catheter system **12**, the separating diaphragm **39**A may alternatively be incorporated into any of the following catheter systems described herein: catheter systems **200**, **300**, **400**, **500**, **600**, **600'**.

Also, while the above described working catheters **42**, **303**, **304**, **404**, **506**, **508**, **606** were shown as only having a single hole or orifice defined in its distal segment through which fluid may be advanced, it should be appreciated that the distal segment of any of such working catheters may have two or more holes defined in its distal segment each through which fluid may be advanced. For example, the distal segment of any one of such working catheters may have a single distal end hole (such as the distal orifice **336** of FIG. **14**) and four additional holes defined in the sidewall of the distal segment, wherein each of the four additional holes is spaced apart from the distal end hole in the proximal direction by a distance.

Additionally, while the above-described catheter system **600** was described as being implanted in the body **14** so that a proximal portion of such respective catheter system is located external to the body **14** and the remainder of such respective catheter system is located within the body **14** (as shown in FIG. **26**), such catheter system **600** could be implanted entirely within the body and still achieve some of the advantages of the present invention. More particularly, such respective catheter system **600** could be configured as a subcutaneous port catheter system **900** having a retractable inner catheter **902** as shown in FIGS. **30–31**. The subcutaneous port catheter system **900** would be implanted entirely beneath the skin **20** of the body **14** within the subcutaneous tissue **22** (see FIGS. **30–31**). The subcutaneous port catheter system **900** further includes a reservoir **904** defining a chamber **906**, and a septum **908** positioned over the chamber **906**. A funnel **907** is attached to the proximal end of the retractable inner catheter **902**. The funnel **907** is located within the reservoir **904** and further is in fluid communication with the retractable inner catheter **902** so that fluid advanced within the funnel **907** subsequently advances into the retractable inner catheter **902**. A spring **909** is positioned around the proximal end portion of the retractable inner catheter **902**. Movement of the funnel **907** in the direction of arrow **911** causes to the spring **909** to compress. The subcutaneous port catheter system **900** also includes a guide catheter **916** which is attached to the reservoir **904**. The guide catheter **916** may include a distal valve **917**. During use, the subcutaneous port catheter system **900** would be implanted in the body **14** so that a distal portion of each of the retractable inner catheter **902** and the guide catheter **916** would extend into the vascular system **24** (see FIGS. **30–31**) in a manner similar to the manner in which catheter system **600** extends into the vascular system in FIG. **26**. Further during use, a needle **918** would be advanced through the skin **20** and the subcutaneous tissue **22** and further through the septum **908** so as to position its distal end in the chamber **906** (see FIG. **31**). During such advancement, the needle **918** would contact the funnel **907** so as to compress the spring **909** thereby causing a distal orifice of the retractable catheter **902** to be advanced out of a distal orifice of the guide catheter **916**. Thereafter, fluid may be infused through the needle **918** into the vascular system **22** with the subcutaneous port catheter system **900**. The needle **918** may then be withdrawn from the chamber **906** and removed from the body **14**. Note that movement of the needle from the chamber **906** in the direction opposite to arrow **911** allows the spring **909** to move the funnel **907** back to its position shown in FIG. **30**. Such movement of the funnel in **907** causes the distal orifice of the retractable inner catheter **902** to be advanced back within the interior of the guide catheter **916** as shown in FIG. **30**.

Obviously, the subcutaneous port catheter system **900** may be modified in a similar manner to the modifications discussed above with respect to the abovedescribed single-lumen catheter system **600**. For example, all the possible modifications and alternatives discussed above in the section entitled "*VII. Conclusion*" which relate to catheter system **600** are applicable to the catheter system **900**.

In addition, the above-described dual-lumen catheter systems (e.g. catheter systems **12**, **200**, **300**, **400**, and **500**) may be modified to incorporate any of the features of the subcutaneous port catheter system **900**.

VIII(a). Catheter System **700**

FIGS. **32–35** show yet another catheter system **700** which incorporates the features of the present invention therein. The catheter system **700** includes a guide catheter **702** and a retractable conduit assembly **704**.

The retractable conduit assembly **704** includes a tube segment **705** through which fluid such as blood may be advanced. The tube segment includes a proximal orifice **708** and a distal orifice **728**. The retractable conduit assembly **704** further includes a pusher **706** attached to the tube segment **705**. The retractable conduit assembly **704** further includes a rotatable cap **710** which is attached to the pusher **706**. The rotatable member **710** includes a set of internal threads **732**.

The pusher **706** is attached to a sidewall of the tube segment as shown in FIG. **34** so as not to interfere with fluid flow entering or exiting a proximal orifice **708** of the tube segment **705**. The pusher **706** may be made of a plastic member having sufficient beam strength to advance the tube segment **705** from its position shown in FIG. **32**, through a portion of the guide catheter **702**, and to its position shown in FIG. **33**. Alternatively, the pusher **706** may be made from a metal wire such a guidewire which is commonly used to assist in the advancement of catheters within the vascular system of a patient. Of course, such metal wire would also need to possess sufficient beam strength to advance the tube segment **705** from its position shown in FIG. **32** to its position shown in FIG. **33**.

The pusher **706** may include a swivel **712** interposed between an upper pusher portion **706**U and a lower pusher portion **706**L as shown in FIG. **35**. The swivel **712** allows the upper pusher portion **706**U to freely rotate relative to the lower pusher portion **706**L. This feature allows the rotatable cap **710** to be easily rotated in relation to the guide catheter **702** so as to move the tube segment **705** between its position shown in FIG. **32** and its position shown in FIG. **33** without causing the lower pusher portion **706**L to be rotated in a similar manner. The swivel **712** may be located at any position along the length of the pusher **706**.

The guide catheter **702** has a common lumen **716** which extends through a lower portion of the guide catheter **702** as

shown in FIGS. **32–33**. The common lumen **716** defines a distal guide orifice **718**. The guide catheter **702** further includes an upper main lumen **720** and a sideport lumen **722** as shown in FIGS. **32–33**.

It should be appreciated that when the retractable conduit assembly **704** is located in its position shown in FIG. **33**, fluid may be advanced through a flow path which includes (i) a proximal orifice **717** of the branch of the guide catheter **702** that defines the sideport lumen **722**, (ii) the sideport lumen **722**, (iii) the common lumen **716**, (iv) the proximal orifice **708** of the tube segment **705**, (v) a tube lumen **726** of the tube segment **705**, and (vi) the distal orifice **728** of the tube segment **705**.

According to one preferred manner of using the catheter system **700**, the tube segment **705** of the retractable conduit assembly **704** is initially located entirely within the guide catheter **702** as shown in FIG. **32**. (Note that FIG. **32** shows the catheter system **700** located in a retracted or stowed position). Thereafter, it may be desirable to perform a medical procedure, such as a TPN administration session. In order to perform such a procedure, the retractable conduit assembly **704** must be moved from its position shown in FIG. **32** to its position shown in FIG. **33**. (Note that FIG. **33** shows the catheter system **700** located in an extended or operative position). In order to achieve such movement, the rotatable cap **710** is continuously rotated by a user in a first direction until it moves from its position shown in FIG. **32** to its position shown in FIG. **33**. Note that such movement is achieved due to the cooperation of the set of internal threads **732** of the rotatable member **710** and a proximal flange **736** defined on the guide catheter **702** at the proximal orifice **717**. The rotatable cap **710** is provided with a gripping member **719** to facilitate rotation of the rotatable member **710** by the user. Further, a stop **721** is provided on the guide catheter **702** to limit rotation of the rotatable cap **710**. Also, the rotatable cap **710** is provided with a retaining ring **723** which functions to prevent the rotatable cap **710** from becoming separated from the guide catheter **702** due to over rotation of the rotatable cap **710** in relation to the guide catheter **702**. After the retractable conduit assembly **704** is moved to its position shown in FIG. **33**, the medical procedure (such as a TPN administration session) is performed. After the TPN administration session is completed, the retractable conduit assembly **704** is moved back to its position shown in FIG. **32**. Of course, in order to achieve such movement, the rotatable cap **710** is continuously rotated (in a direction opposite to the first direction) until it moves from its position shown in FIG. **33** to its position shown in FIG. **32**.

Referring again to FIGS. **32** and **33**, the guide catheter **702** has a tissue ingrowth member **730** secured to an outer surface thereof. Tissue ingrowth member **730** is substantially identical to tissue ingrowth member **38** described hereinabove with regard to the catheter system **12**.

While FIGS. **32–35** show one particular type of mechanism to lock the retractable conduit assembly **704** to the guide catheter **702** in either its stowed position as shown in FIG. **32** or its operative position as shown in FIG. **33**, many other types of locking mechanisms may be used to carry out the present invention. For example, any of the plurality of locking mechanisms **56** described hereinabove with regard to the catheter system **12** may be used to lock the retractable conduit assembly **704** to the guide catheter **702** in either its stowed position as shown in FIG. **32** or its operative position as shown in FIG. **33**.

The guide catheter **702** further includes a distal blood flow valve **740** positioned within the common lumen **716**, and a proximal blood flow valve **742** positioned within the sideport lumen **722** as shown in FIGS. **32–33**. The blood flow valves **740** and **742** are substantially identical to the blood flow valves **37** and **39** which were described hereinabove with regard to the catheter system **12**.

Referring again to FIGS. **32–35**, the tube segment **705** of the retractable conduit assembly **704** defines the tube lumen **726** through which fluid is advanced. The tube lumen **726** defines the proximal orifice **708** and the distal orifice **728**. The distal orifice **728** is defined in a distal portion **744** of the tube segment **705**.

A clamp **746** is positioned on the guide catheter **702** which functions to prevent fluid flow through the upper main lumen **720** when desired. The clamp **746** is substantially identical in construction and function to the clamps **62**, **64** discussed hereinabove with regard to the catheter system **12**.

The catheter system **700** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the catheter system **12** within the body **14** (e.g. by the tunneled catheter technique). While in the body **14**, the locking structure possessed by the retractable conduit assembly **704** and the guide catheter **702** functions to lock the retractable conduit assembly **704** to the guide catheter **702** in either its stowed position (FIG. **32**) or its operative position (FIG. **33**).

It should be appreciated that FIG. **32** shows the retractable conduit assembly **704** locked to the guide catheter **702** in the stowed position. While the retractable conduit assembly **704** is locked in the stowed position in the patient's body **14** between TPN administration sessions, the distal orifice **728** of the tube segment **705** would be isolated from contact with the blood flow in the superior vena cava **32**. FIG. **33** shows the retractable conduit assembly **704** locked to the guide catheter **702** in the operative position. While the retractable conduit assembly **704** is locked in the operative position during performance of a TPN administration procedure, the distal orifice **728** of the tube segment **705** would be positioned within the blood flow in the superior vena cava **32**.

Also, please note that the tube segment **705** of the catheter system **700** contacts the blood located in the vascular system **24** for a substantially reduced amount of time in comparison to the amount of time a conventional catheter (which is used for TPN administration) is contacted by blood located in the vascular system. Accordingly, the physical structure of the tube segment **705** of the catheter system **700** may be substantially the same or similar to the physical structure of a conventional short-term catheter for the same reasons hereinabove discussed in regard to the dialysis catheter **42** of the catheter system **12** in section 1(b) entitled "Performance of a Dialysis Session with the Catheter System **12**".

VIII(b). Further Discussion Regarding Catheter System **700**

The catheter system **700** may be modified in a similar manner to the modifications discussed above with respect to the catheter system **600**. In particular, the modifications and alternatives of the catheter system **600** discussed above with respect to the catheter system **600'** is applicable to the catheter system **700**. Moreover, all the possible modifications and alternatives discussed above in the section entitled "*VII. Conclusion*" which relate to catheter system **600**, and **600'** are applicable to the catheter system **700**.

In addition, certain of the above-described dual-lumen catheter systems (e.g. catheter systems **12**, **200**, **300**, **400**, and **500**) may be modified to incorporate the features of the catheter system **700**. For example, the catheter system **400** may be modified to utilize a retractable conduit assembly similar to the retractable conduit assembly **704** instead of utilizing working catheter **404**. Of course, the guide catheter

402 would need to be modified to include a sideport lumen which would extend from the branch of the guide catheter 402 in which the proximal valve 424 is located.

It should be appreciated that catheter systems 12, 200, 300, 400, 500, 600, 600', and 700 set forth at different locations above are configured and used accordingly to a common theme. Such common theme is to provide a catheter system which includes some type of conduit having a distal orifice through which fluid can be advanced, wherein the distal orifice can be directly exposed to blood in the vascular system (or other bodily fluids outside of the vascular system) during a medical procedure, and thereafter the distal orifice can be shielded by a protective structure whereby the distal orifice of the conduit is not directly exposed to blood in the vascular system (or other bodily fluids outside of the vascular system) when a medical procedure is no longer being performed by the catheter system, but yet when the catheter system is still located within the body (e.g. the vascular system) for a period of time (e.g. for several weeks or months as is the common time period in the case of a long term catheter system). For example, in the case of the catheter system 12 of FIGS. 1–11, the conduit is the catheter 42, while in the case of the catheter system 700 of FIGS. 32–35, the conduit is the tube segment 705. In both of these cases, selective shielding of the distal orifice of the conduit 42, 705 from bodily fluid, such as blood in the vascular system, effectively and conveniently reduces the likelihood that the partial or total occlusion of the fluid path of the respective catheter system would occur due to, for example, blood clot buildup.

IX. Catheter System 800

Another catheter system 800 which incorporates the features of the present invention therein is shown in FIGS. 36, 36A–B, 37, 37A, 38A, 38B, 39, 39A–C, 40, and 40A–D. The catheter system 800 includes a guide catheter 34 (see FIG. 36) and a working catheter 42 (see FIG. 37). The catheter system 800 is somewhat similar to the catheter system 12. Thus, the same reference numerals are used in FIGS. 36, 36A–B, 37, 37A, 38A, 38B, 39, 39A–C, 40, and 40A–D to designate common components which were previously discussed with regard to FIGS. 1–11. Moreover, the description of the components of the catheter system 800 which are common to the catheter system 12 will not be undertaken since they are designated with common reference numerals and such components have been previously described hereinabove. In addition, the guide catheter 34 of the catheter system 800 is placed within the body 14 in substantially the same manner as was described hereinabove with respect to the placement of the guide catheter 34 of the catheter system 12 within the body 14 (e.g. by the tunneled catheter technique).

However, the catheter system 800 differs from the catheter system 12 in that the guide catheter 34 of the catheter system 800 does not possess a distal blood flow valve positioned within the guide lumen 36. Rather, the guide catheter 34 of the catheter system 800 includes a duckbill valve 802 positioned external to the guide lumen 34 just below the distal guide orifice 40 as shown in FIG. 36.

Another difference between the catheter system 800 and the catheter system 12 is that the guide catheter 34 of the catheter system 800 includes a stainless steel wire coil 804 which is cylindrically wound and extends the entire length of a segment 806 of the guide catheter 34 as shown in FIGS. 36 and 36B. Note that for clarity of description only a proximal portion of the segment 806 is shown possessing the wire coil 804. Further, the entire outer surface of the segment 806 of the guide catheter 34 has positioned thereon a nylon material 808 such as PEBAX. PEBAX is a tradename, commonly known to one skilled in the art, for a type of nylon polymer which is commonly used in the medical device industry for the manufacture of catheters. Moreover, the inner surface of the guide catheter 34 of the catheter system 800 which defines the guide lumen 36 may have positioned thereon a Teflon coating 810. The Teflon coating 810 may facilitate sliding of the working catheter 42 relative to the guide catheter 34 during movement of the working catheter between its operative position (shown in FIG. 38A) and its stowed position (shown in FIG. 38B).

Alternatively, instead of the wire coil 804 being made of stainless steel, the wire coil 804 may be made from another metallic material such as NITINOL. NITINOL is a tradename, commonly known to one skilled in the art, for a type of metallic material that is commonly used in the medical device industry in the manufacture of medical devices. The thickness (i.e. the outer diameter) of the strand of wire that makes up the wire coil 804 may be uniform as it extends from the proximal end of the segment 806 to the distal end of the segment 806. Alternatively, certain portion(s) of the strand of wire which makes up the wire coil 804 may possess a first larger thickness while other portion(s) may possesses a second smaller thickness. For example, the strand of wire that makes up the wire coil 804 which is required to be bent into a U-shaped orientation when the guide catheter 34 of the catheter system 12 is implanted in the patient's body 14 (see e.g. FIG. 9) may possess the first larger thickness, while the strand of wire that makes up the wire coil 804 which is linearly oriented on each side of the U-shaped portion may possess the second smaller thickness. This variation in the thickness of the strand of wire that makes up the wire coil 804 may reduce the likelihood of kinking or other deformation of the guide catheter 34 during implantation and use of the guide catheter 34. Also, it should be noted that the more tightly the strand of wire which makes up the wire coil 804 is wound (i.e. the more turns per linear inch), the less likely the guide catheter 34 will kink or otherwise deform during implantation and use of the guide catheter 34.

Still another difference between the catheter system 800 and the catheter system 12 is that the locking mechanism 56 of the catheter system 800 has a somewhat different physical configuration when compared to the locking mechanism 56 of the catheter system 12. In particular, FIGS. 36, 36A–B, 37, 37A, 38A and 38B show the physical configuration of the locking mechanism 56. One point of distinction is that each of the locking component of the guide catheter 34 and the locking component of the working catheter 42 possesses finger grips. More specifically, the locking component of the guide catheter 34 possesses a first finger grip 812, while the locking mechanism of the working catheter 42 possesses a second finger grip 814. These grips form the basis of a supplemental locking system 816 and facilitate user actuation of the working catheter 42 between its operative position (shown in FIG. 38A) and its stowed position (shown in FIG. 38B).

The locking component of the working catheter 42 includes a retaining ring 819 positioned within such locking component near the finger grip 814 as shown in FIG. 37. The retaining ring 819 functions to prevent the locking component of the working catheter 42 from becoming separated from the locking component of the guide catheter 34 due to over rotation between these two components. For example, if the working catheter 42 is advanced from its position shown in FIG. 38A to its position shown in FIG. 38B, further advancement in such direction is prevented due to contact

between a shoulder **823** of the guide catheter **34** (see FIG. **36**) and the retaining ring **821** of the working catheter **42** (see FIG. **37**).

Turning to the supplemental locking system **816**, each of the finger grips **812**, **814** have a plurality of grooves **818** defined therein (see FIG. **39**). The supplemental locking system **816** includes a locking clip **820** having a pair of nubs **822** as shown in FIGS. **39**A, **39**B, and **39**C. In order to further lock the working catheter **42** in a fixed position relative to the guide catheter **34**, the locking clip **820** is applied over the finger grips **812**, **814** when the grooves **818** of the first finger grip **812** are aligned with the grooves **818** of the second finger grip **814** as shown in FIG. **39**. When so aligned, the nubs **822** are received into the grooves **818** of finger grips **812**, **814** as shown in FIG. **39**C so as to prevent relative rotation between the working catheter **42** and the guide catheter **34**.

Another supplemental locking system **824** is shown in FIGS. **40**, **40**A, **40**B, **40**C, and **40**D. The supplemental locking system **824** includes a slider **826** which is securely positioned within a first recess **828** defined in the first finger grip **812** and a second recess **830** defined in the second finger grip **814**. When the slider **826** is moved to its leftmost position in the direction of arrow **832**, the working catheter **42** can be rotated in relation to the guide catheter **34**. When the slider **826** is located in its position as shown in FIG. **40**, the slider **826** prevents rotation of the working catheter **42** in relation to the guide catheter **34**.

Yet another distinction between the catheter system **800** and the catheter system **12** is that the working catheter **42** includes a first segment **815** which possesses a first degree of hardness (having a first durometer rating), and a second segment **817** which possesses a second degree of hardness (having a second durometer rating) as shown in FIG. **37**. Providing the first segment **815** with relatively increased hardness may facilitate the slidability of the working catheter **42** in relation to the guide catheter **34**. The difference in the degree of hardness between the first segment **815** and the second segment **817** may be created by manufacturing the first segment **815** with a first material possessing a first resin-to-nylon content ratio, while manufacturing the second segment **817** with a second material possessing a second resin-to-nylon content ratio which is different from the first resin-to-nylon content ratio. Note that the degree of hardness of a catheter depends on the percentage of resin used in comparison to the percentage of nylon used in the manufacturing process of the catheter. Resin is a filler material. The more resin used, the softer the catheter. The more nylon used, the harder the catheter. A catheter can be made of two different segments having different degrees of hardness by thermally fusing the two catheter segments together at a transition area. This transition area may be located at any position along the length of the catheter. With regard to catheter system **800**, the first segment **815** of the working catheter **42** could be configured to possess a higher degree of hardness in order to provide better slidability of the working catheter **42** in relation to the guide catheter **34**. Moreover, since the distal end segment of the working catheter **42** possesses a lesser degree of hardness, such distal end is advantageously softer in order to minimize trauma to the vascular system in which it is used. For example, the distal end segment of the working catheter **42** which is advanced out of the distal guide orifice **40** of the guide catheter **34** according to one preferred method of the present invention would possess a relatively soft configuration in order to minimize trauma to the vascular system **24**.

Alternatively, the original dialysis catheter **42** may be manufactured such that its first segment **815** and its second segment **817** possess an identical degree of hardness (or identical durometer rating).

Obviously, the catheter system **800** may be modified in a similar manner to the modifications discussed above with respect to the above-described duallumen catheter systems (e.g. catheter systems **12**, **200**, **300**, **400**, and **500**). For example, all the possible modifications and alternatives discussed above in the section entitled "*VII. Conclusion*" which relate to catheter system **12**, **200**, **300**, **400**, and **500** are applicable to the catheter system **800**.

In addition, the above-described dual-lumen catheter systems (e.g. catheter systems **12**, **200**, **300**, **400**, and **500**) and the single lumen catheter systems (e.g. catheter systems **600**, **600'**, **700** and **900**) may be modified to incorporate any of the features of the catheter system **800**.

X. Catheter System **1000**

Another catheter system **1000** which incorporates the features of the present invention therein is shown in FIGS. **41**–**45**. The catheter system **1000** includes a retractable sheath assembly **1034** and a working catheter **1042** which are attached together. The working catheter **1042** of the catheter system **1000** is somewhat similar to the working catheter **42** of the catheter system **12**. Thus, many of the same reference numerals are used in FIGS. **41**–**45** to designate common components of the working catheters **42**, **1042** which were previously discussed with regard to FIGS. **1**–**11**. Moreover, the description of the components of the working catheter **1042** of the catheter system **1000** which are common to the catheter system **12** will not be undertaken since they are designated with common reference numerals and such components have been previously described hereinabove. In addition, the guide catheter **1034** of the catheter system **1000** is placed within the body **14** in substantially the same manner as was described hereinabove with respect to the placement of the guide catheter **34** of the catheter system **12** within the body **14** (e.g. by the tunneled catheter technique).

However, the catheter system **1000** differs from the catheter system **12** in that the catheter system **1000** does not possess a guide catheter exactly the same as the guide catheter **34** of the catheter system **12**, but rather possesses the retractable sheath assembly **1034**. The retractable sheath assembly **1034** includes an outer guide tube **1036** and an inner retractable conduit **1038**. The outer guide tube **1036** includes a tissue ingrowth member **1043** secured to an outer surface thereof. Tissue ingrowth member **1043** is substantially identical to tissue ingrowth member **43** described hereinabove with regard to the catheter system **12**.

It should be appreciated that the inner retractable conduit **1038** is movable in relation to the guide tube **1036** from its position shown in FIG. **41** (see also FIG. **43**) to its position shown in FIG. **42** (see also FIG. **44**). Note that during operation of the catheter system **1000**, the working catheter **1042** is fixed in relation in relation to the outer guide tube **1036** (e.g. the working catheter **1042** does not move axially in relation to the outer guide tube **1036**). Rather, in order to shield the distal orifices **50**, **54** so that such distal orifices are not directly exposed to blood in the vascular system **24** (or other bodily fluids outside of the vascular system) when a medical procedure is no longer being performed by the catheter system **1000**, the inner retractable conduit **1038** is movable in relation to the working catheter **1042** (and also in relation to the guide tube **1036**). In particular, the inner retractable conduit **1038** is movable from its position shown in FIG. **41** (in which it effectively stows the distal working segment **55** of the working catheter **1042** therein) to its position shown in FIG. **42** (in which it is withdrawn within

the outer guide tube **1036** so as to expose the distal working segment **55** of the working catheter **1042** in order for a medical procedure to be performed on the patient (e.g. a dialysis procedure).

The retractable sheath assembly **1034** includes an actuator **1044** which is mechanically coupled to the retractable inner conduit **1038**. Movement of the actuator **1044** from its position shown in FIG. **41** to its position shown in FIG. **42** causes the retractable inner conduit **1038** to move from its position shown in FIG. **41** to its position shown in FIG. **42**. In order to guide movement of the actuator **1044**, a guide slot **1046** is provided in the outer guide tube **1036**.

One or more supplemental locking mechanisms (not shown) may be used to further lock the actuator **1044** at either of its positions shown in FIGS. **41–42**.

The catheter system **1000** may be used to perform any of the medical procedures described hereinabove as being performed by the catheter system **12** including but not limited to dialysis procedures. Moreover, the catheter system **1000** may be modified in a similar manner to the modifications discussed above with respect to the above-described dual-lumen catheter systems (e.g. catheter systems **12, 200, 300, 400, 500,** and **800**) For example, all the possible modifications and alternatives discussed above in the section entitled "*VII. Conclusion*" which relate to catheter systems **12, 200, 300, 400,** and **500** are applicable to the catheter system **1000**.

In addition, the above-described dual-lumen catheter systems (e.g. catheter systems **12, 200, 300, 400, 500, 800**) and the single lumen catheter systems (e.g. catheter systems **600, 600', 700,** and **900**) may be modified to incorporate any of the features of the catheter system **1000**. Alternatively, the catheter system **1000** may be modified to incorporate any of the features of the catheter systems **12, 200, 300, 400, 500, 600, 600', 700, 800,** and **900**.

Moreover, it should be appreciated that any one of the catheter systems **12, 200, 300, 400, 500, 600, 600', 700, 800, 900 1000** described in this document may incorporate any one or more features of another catheter system (i.e. **12, 200, 300, 400, 500, 600, 600', 700, 800, 900 1000**) described in this document.

XI. Hybrid Removable/Retractable Catheter System **1200**

Another catheter system **1200** that incorporates the features of the present invention therein is shown in FIG. **46**. The catheter system **1200**, which may be referred to a hybrid catheter system, includes an inner retractable catheter system **1202** and an outer guide catheter **1204**. The inner catheter system **1202** is constructed and used in the same manner as the catheter system **12** that is disclosed in U.S. Pat. No. 6,190,371 issued to Maginot et al., except for two differences. The entire disclosure of U.S. Pat. No. 6,190,371 is hereby incorporation by reference. The first difference is that the tissue ingrowth member **43** disclosed in the '371 patent would not be included on the retractable inner catheter system **1202**. The second difference is that the inner retractable catheter system **1202** has a locking mechanism **66'** which is substantially identical in construction and use as the second locking mechanism **66** of the catheter system **16** disclosed in U.S. Pat. No. 6,156,016 issued to Maginot (see e.g. FIG. **6**). The entire disclosure of U.S. Pat. No. 6,156,016 is hereby incorporation by reference.

The outer guide catheter **1204** is constructed and used in the same manner as the guide catheter **32** disclosed in U.S. Pat. No. 6,156,016 (e.g. see FIG. **4A**) except for one difference. The one difference is that the outer guide catheter **1204** possesses a larger inner diameter to accommodate the positioning of the inner retractable catheter system **1202** therein as shown in FIG. **46**.

The hybrid catheter system **1200** is implanted and used in the same manner as described with respect to the implantation and use of the catheter system **12** that is disclosed in U.S. Pat. No. 6,190,371. However, if for any reason the inner retractable catheter system **1202** becomes dysfunctional, the inner retractable catheter system **1202** could be replaced with a new inner retractable catheter system that is identical in construction and function to the inner retractable catheter system **1202**. The inner retractable catheter system **1202** may be replaced in the same manner as described with respect to the replacement of the dialysis catheter **48** with the replacement dialysis catheter **58** as disclosed in U.S. Pat. No. 6,156,016.

Obviously, the catheter system **1200** may be modified in a similar manner to the modifications discussed above with respect to all of the above-described catheter systems. Moreover, all of the above-described catheter systems may be modified to incorporate any of the features of the catheter system **1200.**

XII. Catheter System **1300**

Another catheter system **1300** which incorporates the features of the present invention therein is shown in FIGS. **47–51**. The catheter system **1300** is identical to the catheter system **12** described above and shown in FIGS. **1–11**, except that the catheter system **1300** possesses yet another alternative locking mechanism **56'** to the locking mechanism **56** of FIGS. **4–11**. In particular, the locking mechanism **56'** includes a wall **1302** having a number of detent recesses **1304** defined therein. The locking mechanism **56'** may further include an arm assembly **1306**. The arm assembly **1306** includes a ring **1308** which is positioned around and secured to the working catheter **42** of the catheter system **1300**. The arm assembly **1306** further includes an arm **1310** connected to the ring **1308**. The arm **1310** includes a tang **1312** located on a proximal end thereof.

During use of the catheter system **1300,** the tang **1312** cooperates with the detent recesses **1304** so as to selectively lock the working catheter **42** in relation to the guide catheter **34** at either a stowed position (see FIG. **10**) or at an operative position (see FIG. **11**). FIG. **48** (and FIG. **50**) show the locking mechanism **56'**when the working catheter **42** is locked to the guide catheter **34** in the operative position. FIG. **49** (and FIG. **51**) show the locking mechanism **56'** when the working catheter **42** is locked to the guide catheter **34** in the stowed position.

The guide catheter **34** of the catheter system **1300** includes a lock housing **1314**. The lock housing **1314** includes a number of walls, including wall **1302**, which enclose the components of the locking mechanism **56'**. The housing **1314** further includes a door **1316** having a handle **1318**. The door **1316** is pivotable from its open position shown in FIG. **48** (and FIG. **50**) to its closed position shown in FIG. **49** (and FIG. **51**). The housing **1316** further includes a stop **1320** configured to retain the door **1316** in its closed position.

In order to further seal a lower portion of the working catheter **42** (i.e. the portion of the working catheter **42** located within the lock housing **1314** and all portions of the working catheter **42** distal thereto) within the guide catheter **34**, an accordion shaped seal **1322** is positioned completely around a segment of the arm **1310** and attached to the ring **1308** at its distal end. The accordion shaped seal **1322** is attached to the housing at its proximal end as shown in FIGS. **48–49**. Alternatively, as shown in FIGS. **50–51**, the accordion seal **1322** may be replaced with a flexible diaphragm seal **1323** that completely surrounds the working catheter **42**. In particular, the diaphragm seal **1323** is annular

shaped and is attached at its outer periphery to the inner surface of the lock housing **1314** of the guide catheter **34**, and further is attached at its inner periphery to the outer surface of the working catheter **42**. The flexible diaphragm seal **1323** would have a substantially similar configuration and function to the flexible separating diaphragm **39**A of FIG. **8**A discussed hereinabove.

It should be noted that the working catheter **42** includes a coiled or helical segment **1324** that can be extended from its coiled configuration shown in FIG. **49** to its substantially straight configuration shown in FIG. **48**. The segment **1324** is configured to retain its coiled shape as shown in FIG. **49** absent application of any external force thereto. The segment **1324** is formed to possess such a coiled shape in a similar manner to that commonly used in the medical device manufacturing arts to provide a pre-formed shape to a catheter (e.g. a pig-tailed catheter).

In operation, if a user applies downward force to the arm **1310** in order to move the working catheter **42** from its stowed position (see FIG. **10**) to its operative position (see FIG. **11**), the coiled segment moves from its coiled configuration (see FIG. **49**) to its substantially straight configuration (see FIG. **48**). Thereafter, the tang **1312** cooperates with the respective detent recess **1304** in order to retain the coiled segment **1324** in its substantially straight configuration as shown in FIG. **48** (and FIG. **50**). If a user desires to return the working catheter from its operative position (see FIG. **11**) to its stowed position (see FIG. **10**), the user simply lifts the tang **1312** out of the respective detent recess **1304** and pulls upwardly until the arm is located at its position shown in FIG. **49**. As the arm **1310** moves upwardly, the coiled segment springs back to its coiled configuration (see FIG. **49**) due to the inherent spring-like characteristics of the preformed coiled segment **1324**.

Moreover, it should be appreciated that the locking mechanism **56'** may be modified to incorporate a supplemental force transmitting mechanism (not shown) in order to move the working catheter **42** in relation to the guide catheter **34** from its stowed position (see FIG. **10**) to its operative position (see FIG. **11**). In particular, such supplemental force transmitting mechanism may include a hydraulic or pneumatic device (not shown) that may be substituted for arm **1310**. The hydraulic or pneumatic device would be coupled between an inner surface of the lock housing **1314** at a location L (see FIG. **50**) and the ring **1308**. The hydraulic or pneumatic device would include a rod and a cylinder (not shown). The hydraulic or pneumatic device would be operable to extend and retract the rod out of the cylinder to move the working catheter **42** in relation to the guide catheter **34**. The hydraulic or pneumatic device would be actuated by a syringe that would be coupled to the cylinder of the hydraulic or pneumatic device via tubing.

XIII. Catheter System **1400**

Another catheter system **1400** that incorporates the features of the present invention therein is shown in FIGS. **52**–**53**. The catheter system **1400** is somewhat similar to the catheter system **12** discussed above. Thus, the same reference numerals are used in FIGS. **52** and **53** to designate common components that were previously discussed with regard to FIGS. **1**–**11**. Moreover, the description of the components of the catheter system **1400** which are common to the catheter system **12** will not be undertaken since they are designated with common reference numerals and such components have been previously described hereinabove.

The catheter system **1400** of FIGS. **52** and **53** is used in substantially the same manner as herein described with respect to the catheter system **12**. Moreover, the catheter system **1400** of FIGS. **52** and **53** is exactly the same in construction and configuration as the catheter system **12** shown in FIGS. **1**–**11**, with the exception that the locking mechanism **56'** is substituted for locking mechanism **56**. Another exception is that the guide catheter **34** of the catheter system **1400** is much shorter in length than the guide catheter **34** of the catheter system **12**, while the working catheter **42** of the catheter system **1400** of FIGS. **52** and **53** is the same length as the working catheter **42** of the catheter system **12**. (For example, compare FIGS. **52** and **53** with FIG. **9**). In particular, the length of the guide catheter **34** of the catheter system **1400** of FIGS. **52** and **53** is such that after it is placed in the body **14** as shown in FIGS. **52** and **53**, its distal guide orifice **1402** is located entirely outside of the vascular system **24** in the subcutaneous tissue **22** preferably two centimeters proximal to the venotomy **76**. Moreover, in this embodiment of the present invention shown in FIGS. **52** and **53**, the distance between the most distal working orifice of the working catheter **42** and the distal guide orifice **1402** of the guide catheter **34** (in its extended configuration as shown in FIG. **53**) is preferably approximately twenty-two centimeters. In contrast, in the embodiment shown in FIGS. **1**–**11**, the distance between the most distal working orifice **54** of the working catheter **42** and the distal guide orifice **40** of the guide catheter **34** is preferably approximately three centimeters.

During operation, the working catheter **42** is able to be moved relative to the guide catheter **34** between its retracted position as shown in FIG. **52** and its extended position as shown in FIG. **53**. More specifically, the most distal working orifice of the working catheter **42** of the catheter system **1400** is located at point P1 within the superior vena cava **32** (see FIG. **52**) when the working catheter is positioned in its retracted position. However, the most distal working orifice of the working catheter **42** is located at point P2 within the superior vena cava **32** (see FIG. **52**) when the working catheter is positioned in its extended position.

It is believed that, during use, a fibrin sheath will form around and envelope the portion of the working catheter **42** of the catheter system **1400** which is located in the vascular system **24** while the working catheter is positioned in its retracted position as shown in FIG. **52**. It is believed that the fibrin sheath will be attached to the wall of the right internal jugular vein **26** near the venotomy where the working catheter enters the vascular system **24**. The working catheter would be located in this retracted position between dialysis sessions. However, it is believed that when the working catheter is moved to its extended position as shown in FIG. **53** in order to carry out a dialysis session, a distal segment of the working catheter **42** will be advanced through a distal end of the fibrin sheath thereby exposing the two working distal orifices of the working catheter **42** to a flow of blood within the superior vena cava **32**. The working catheter **42** will remain in this extended position for a duration of time sufficient to carry out a dialysis session. After the dialysis session is carried out, the working catheter **42** will be moved back to its retracted position as shown in FIG. **52** until another dialysis session is to be carried out.

There is a plurality of advantages of the present invention arising from the various features of each of the catheter systems described herein. It will be noted that alternative embodiments of each of the catheter systems of the present invention may not include all of the features described yet still benefit from at least some of the advantages of such features. Those of ordinary skill in the art may readily devise their own implementations of each of the catheter systems that incorporate one or more of the features of the present

invention and fall within the spirit and scope of the present invention as defined by the appended claims.

It should be appreciated that any of the features of any one catheter system described herein may be used with any of the other catheter systems described herein.

What is claimed is:

1. A method of performing dialysis with a catheter system which includes (i) a working catheter having a distal working orifice, and (ii) a guide catheter having a guide lumen and a distal guide orifice, comprising the steps of:

locking said working catheter in an operative position in which (i) said working catheter extends through said guide lumen of said guide catheter and out of said distal guide orifice of said guide catheter, and (ii) said distal working orifice of said working catheter is positioned outside of said guide catheter;

performing a dialysis procedure including advancing and withdrawing blood through said working catheter while said working catheter is locked in said operative position; and

after said dialysis procedure performing step, locking said working catheter in a stowed position in which (i) said working catheter extends into said guide lumen of said guide catheter, and (ii) said distal working orifice of said working catheter is positioned within said guide lumen of said guide catheter.

2. The method of claim **1**, further comprising the step of advancing a quantity of blood clot dissolving liquid within said guide lumen of said guide catheter when said working catheter is locked in said stowed position.

3. The method of claim **2**, wherein said blood clot dissolving liquid contacts said working catheter at said distal working orifice when said working catheter is locked in said stowed position.

4. The method of claim **3**, wherein said blood clot dissolving liquid includes urokinase.

5. The method of claim **1**, further comprising the step of:

inhibiting advancement of blood into contact with said working catheter at said distal working orifice with a distal valve while said working catheter is locked in said stowed position.

6. The method of claim **5**, wherein said inhibiting step includes the step of inhibiting advancement of blood from a first location outside of said guide lumen to a second location inside of said guide lumen with said distal valve while said working catheter is locked in said stowed position.

7. The method of claim **6**, wherein:

said distal working orifice is positioned on a proximal side of said distal valve when said working catheter is locked in said stowed position, and

said distal working orifice is positioned on a distal side of said distal valve when said working catheter is locked in said operative position.

8. The method of claim **1**, wherein:

said working catheter is a multiple lumen catheter which includes an advancement lumen and a withdrawal lumen, and

said dialysis procedure performing step includes the steps of (i) advancing blood from a proximal end of said working catheter toward a distal end of said working catheter through said advancement lumen, and (ii) withdrawing blood from said distal end of said working catheter toward said proximal end of said working catheter through said withdrawal lumen.

9. The method of claim **1**, wherein:

said working catheter includes a distal working segment in which said distal working orifice is defined,

said distal working segment extends out of said distal guide orifice of said guide catheter so that said distal working orifice is positioned outside of said guide lumen when said working catheter is locked in said operative position, and

said distal working segment is positioned completely within said guide catheter such that said distal working orifice is positioned within said guide lumen when said working catheter is locked in said stowed position.

10. The method of claim **1**, further comprising the steps of:

advancing said guide catheter into a body of a patient so that (i) said distal guide orifice of said guide catheter is positioned within a blood vessel of said body, and (ii) a tissue ingrowth member is positioned in subcutaneous tissue of said body; and

leaving said guide catheter within said body for a period of time sufficient to cause said subcutaneous tissue to become affixed to said tissue ingrowth member,

wherein said tissue ingrowth member is secured to an outer surface of said guide catheter and configured to facilitate fibrous tissue growth therein, and

wherein said guide catheter advancing step is performed prior to said dialysis procedure performing step.

11. A method of performing a series of dialysis procedures on a body of a patient with a catheter system which includes (i) a working catheter having a distal working orifice, and (ii) a guide catheter having a guide lumen and a distal guide orifice, comprising the steps of:

(a) locking said working catheter in an operative position in which (i) said working catheter extends through said guide lumen of said guide catheter and out of said distal guide orifice of said guide catheter, and (ii) said distal working orifice of said working catheter is positioned outside of said guide catheter;

(b) after step (a), performing an initial dialysis procedure on said body of said patient which includes advancing and withdrawing fluid through said working catheter while said working catheter is locked in said operative position, said working catheter being coupled to a dialysis machine during said initial dialysis procedure;

(c) after step (b), locking said working catheter in a stowed position in which (i) said working catheter extends into said guide lumen of said guide catheter, and (ii) said distal working orifice of said working catheter is positioned within said guide lumen of said guide catheter;

(d) after step (c), maintaining said working catheter in said stowed position during an idle period during which said catheter system is decoupled from said dialysis machine, said catheter system being located at least partially within said body of said patient throughout the entirety of said idle period;

(e) after step (d), locking said working catheter in said operative position; and

(f) after step (e), performing a subsequent dialysis procedure on said body of said patient which includes advancing and withdrawing fluid through said working catheter while said working catheter is locked in said operative position, said working catheter being coupled to said dialysis machine during said subsequent dialysis procedure.

12. The method of claim 11, further comprising the step of:

inhibiting advancement of blood into contact with said working catheter at said distal working orifice with a distal valve while said working catheter is locked in said stowed position.

13. The method of claim 12, wherein said inhibiting step includes the step of inhibiting advancement of blood from a first location outside of said guide lumen to a second location inside of said guide lumen with said distal valve while said working catheter is locked in said stowed position.

14. A method of performing dialysis on a body of a patient with a catheter system which includes (i) a conduit having a distal working orifice, and (ii) a guide catheter having a guide lumen and a distal guide orifice, comprising the steps of:

locking said conduit to said guide catheter in an operative position in which said distal working orifice of said conduit is positioned outside of said guide catheter;

performing an initial dialysis procedure including advancing and withdrawing blood through said conduit while said conduit is locked in said operative position; and

after said initial dialysis procedure, locking said conduit to said guide catheter in a stowed position in which said distal working orifice of said conduit is positioned within said guide lumen of said guide catheter.

15. The method of claim 14, further comprising the step of performing a subsequent dialysis procedure including advancing and withdrawing blood through said conduit while said conduit is locked in said operative position, wherein:

said catheter system is at least partially located at least partially within said body continuously between completion of said initial dialysis procedure and commencement of said subsequent dialysis procedure.

16. The method of claim 15, further comprising the step of:

prior to said initial dialysis procedure performing step, attaching said catheter system to said body, wherein said catheter system remains attached to said body continuously between completion of said initial dialysis procedure performing step and commencement of said subsequent dialysis procedure performing step.

17. The method of claim 15, wherein:

said initial dialysis procedure is an initial hemodialysis procedure, and

said subsequent dialysis procedure is a subsequent hemodialysis procedure.

18. The method of claim 15, wherein:

said initial dialysis procedure is an initial peritoneal dialysis procedure, and

said subsequent dialysis procedure is a subsequent peritoneal procedure.

19. The method of claim 18, wherein said conduit is a working catheter.

20. The method of claim 14, further comprising the step of advancing a quantity of blood clot dissolving liquid within said guide lumen of said guide catheter when said conduit is locked in said stowed position.

21. The method of claim 20, wherein said blood clot dissolving liquid contacts said conduit at said distal working orifice when said conduit is locked in said stowed position.

22. The method of claim 21, wherein said blood clot dissolving liquid includes urokinase.

23. The method of claim 14, further comprising the step of:

inhibiting advancement of blood into contact with said conduit at said distal working orifice with a distal valve while said conduit is locked in said stowed position.

24. The method of claim 23, wherein said inhibiting step includes the step of inhibiting advancement of blood from a first location outside of said guide lumen to a second location inside of said guide lumen with said distal valve while said conduit is locked in said stowed position.

25. The method of claim 24, wherein:

said distal working orifice is positioned on a proximal side of said distal valve when said conduit is locked in said stowed position, and

said distal working orifice is positioned on a distal side of said distal valve when said conduit is locked in said operative position.

26. The method of claim 14, wherein:

said conduit is a multiple lumen catheter which includes an advancement lumen and a withdrawal lumen, and

said initial dialysis procedure performing step includes the steps of (i) advancing blood from a proximal end of said conduit toward a distal end of said conduit through said advancement lumen, and (ii) withdrawing blood from said distal end of said conduit toward said proximal end of said conduit through said withdrawal lumen.

27. The method of claim 14, wherein:

said conduit includes a distal working segment in which said distal working orifice is defined,

said distal working segment extends out of said distal guide orifice of said guide catheter so that said distal working orifice is positioned outside of said guide lumen when said conduit is locked in said operative position, and

said distal working segment is positioned completely within said guide catheter such that said distal working orifice is positioned within said guide lumen when said conduit is locked in said stowed position.

28. A method of performing a series of medical procedures on a body of a patient, comprising the steps of:

securing a catheter system to said body using a tunneled catheter technique;

performing an initial medical procedure on said body after said securing step, said initial medical procedure including advancing fluid through a distal orifice of a conduit of said catheter system, and said distal orifice being located outside of a guide lumen of a guide catheter of said catheter system during said initial medical procedure performing step;

after said initial medical procedure performing step, locking said distal orifice of said conduit within said guide lumen of said guide catheter of said catheter system; and

performing a subsequent medical procedure on said body after said locking step, said subsequent medical procedure including advancing fluid though said distal orifice of said conduit of said catheter system, and said distal orifice being located outside of said guide lumen of said guide catheter of said catheter system during said subsequent medical procedure performing step.

29. The method of claim 28, wherein:

said initial medical procedure is an initial dialysis procedure, and

said subsequent medical procedure is a subsequent dialysis procedure.

30. The method of claim 29, wherein:

said initial dialysis procedure is an initial hemodialysis procedure, and

said subsequent dialysis procedure is a subsequent hemodialysis procedure.

31. The method of claim 29, wherein:

said initial dialysis procedure is an initial peritoneal dialysis procedure, and

said subsequent dialysis procedure is a subsequent peritoneal procedure.

32. The method of claim 28, wherein:

said initial medical procedure is an initial plasmapheresis procedure, and

said subsequent medical procedure is a subsequent plasmapheresis procedure.

33. The method of claim 28, wherein:

said initial medical procedure is an initial total parenteral nutrition administration procedure, and

said subsequent medical procedure is a subsequent total parenteral nutrition administration procedure.

34. The method of claim 28, wherein:

said initial medical procedure is an initial chemotherapy administration procedure, and

said subsequent medical procedure is a subsequent chemotherapy administration procedure.

35. The method of claim 28, wherein:

said initial medical procedure is an initial blood transfusion procedure, and

said subsequent medical procedure is a subsequent blood transfusion procedure.

36. The method of claim 28, wherein:

said initial medical procedure is an initial blood sampling procedure, and

said subsequent medical procedure is a subsequent blood sampling procedure.

37. The method of claim 28, wherein said securing step includes the steps of:

advancing said guide catheter into said body so that (i) said distal guide orifice of said guide catheter is positioned within a blood vessel of said body, and (ii) a tissue ingrowth member which is secured to an outer surface of said guide catheter is positioned in subcutaneous tissue of said body; and

leaving said guide catheter within said body for a period of time sufficient to cause said subcutaneous tissue to become affixed to said tissue ingrowth member.

38. The method of claim 28, wherein said catheter system is located within said body continuously between completion of said initial medical procedure performing step and commencement of said subsequent medical procedure performing step.

39. The method of claim 28, wherein said catheter system remains attached to said body continuously between completion of said initial medical procedure performing step and commencement of said subsequent medical procedure performing step.

40. The method of claim 28, further comprising the step of advancing a quantity of blood clot dissolving liquid within said guide lumen of said guide catheter while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

41. The method of claim 40, wherein said blood clot dissolving liquid contacts said conduit at said distal working orifice while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

42. The method of claim 41, wherein said blood clot dissolving liquid includes urokinase.

43. The method of claim 28, further comprising the step of:

inhibiting advancement of blood into contact with said conduit at said distal working orifice with a distal valve while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

44. The method of claim 43, wherein said inhibiting step includes the step of inhibiting advancement of blood from a first location outside of said guide lumen to a second location inside of said guide lumen with said distal valve while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

45. The method of claim 44, wherein:

said distal working orifice is positioned on a proximal side of said distal valve while said distal orifice of said conduit is locked within said guide lumen of said guide catheter, and

said distal working orifice is positioned on a distal side of said distal valve during (i) said initial medical procedure performing step, and (ii) said subsequent medical procedure performing step.

46. The method of claim 28, wherein:

said conduit is a multiple lumen catheter which includes an advancement lumen and a withdrawal lumen, and

said medical procedure performing step includes the steps of (i) advancing blood from a proximal end of said conduit toward a distal end of said conduit through said advancement lumen, and (ii) withdrawing blood from said distal end of said conduit toward said proximal end of said conduit through said withdrawal lumen.

47. The method of claim 28, wherein:

said conduit includes a distal working segment in which said distal working orifice is defined,

said distal working segment extends out of said distal guide orifice of said guide catheter so that said distal working orifice is positioned outside of said guide lumen during said initial medical procedure performing step, and

said distal working segment is positioned completely within said guide catheter such that said distal working orifice is positioned within said guide lumen while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

48. The method of claim 28, wherein:

said guide catheter further has a proximal guide orifice, and

said conduit extends through said proximal guide orifice, said guide lumen, and said distal guide orifice during said initial medical procedure performing step.

49. The method of claim 28, wherein said conduit is a working catheter.

50. A method of performing a series of dialysis procedures on a body of a patient, comprising the steps of:

performing an initial dialysis procedure on said body including advancing blood through a distal orifice of a conduit of a catheter system, and said distal orifice being located outside of a guide lumen of a guide catheter of said catheter system during said initial dialysis procedure performing step;

after said initial dialysis procedure performing step, locking said distal orifice of said conduit within said guide lumen of said guide catheter of said catheter system; and

performing a subsequent dialysis procedure on said body after said locking step, said dialysis procedure including advancing blood though said distal orifice of said conduit of said catheter system, and said distal orifice being located outside of said guide lumen of said guide catheter of said catheter system during said subsequent dialysis procedure performing step.

51. The method of claim **50**, wherein said conduit is located within said body continuously between completion of said initial dialysis procedure performing step and commencement of said subsequent dialysis procedure performing step.

52. The method of claim **50**, further comprising the step of:

prior to said initial dialysis procedure performing step, attaching said catheter system to said body, wherein said working catheter remains attached to said body continuously between completion of said initial dialysis procedure performing step and commencement of said subsequent dialysis procedure performing step.

53. The catheter system of claim **50**, wherein said conduit is a working catheter.

54. The method of claim **50**, wherein:

said initial dialysis procedure is an initial hemodialysis procedure, and

said subsequent dialysis procedure is a subsequent hemodialysis procedure.

55. The method of claim **50**, wherein:

said initial dialysis procedure is an initial peritoneal dialysis procedure, and

said subsequent dialysis procedure is a subsequent peritoneal procedure.

56. The method of claim **50**, wherein said initial dialysis procedure performing step, said locking step, and said subsequent dialysis procedure performing step are each performed while said catheter system is secured to said body using said tunneled catheter technique.

57. The method of claim **52**, wherein said attaching step includes the steps of:

attaching said catheter system to an attachment mechanism which includes at least one extension, and

suturing said at least one extension to said body.

58. The method of claim **52**, wherein said attaching step includes the step of securing said catheter system to said body using a tunneled catheter technique.

59. The method of claim **50**, further comprising the step of advancing a quantity of blood clot dissolving liquid within said guide lumen of said guide catheter while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

60. The method of claim **59**, wherein said blood clot dissolving liquid contacts said conduit at said distal working orifice while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

61. The method of claim **59**, wherein said blood clot dissolving liquid includes urokinase.

62. The method of claim **50**, further comprising the step of:

inhibiting advancement of blood into contact with said conduit at said distal working orifice with a distal valve while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

63. The method of claim **62**, wherein said inhibiting step includes the step of inhibiting advancement of blood from a first location outside of said guide lumen to a second location inside of said guide lumen with said distal valve while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

64. The method of claim **63**, wherein:

said distal working orifice is positioned on a proximal side of said distal valve while said distal orifice of said conduit is locked within said guide lumen of said guide catheter, and

said distal working orifice is positioned on a distal side of said distal valve during (i) said initial dialysis procedure performing step, and (ii) said subsequent dialysis procedure performing step.

65. The method of claim **50**, wherein:

said conduit is a multiple lumen catheter which includes an advancement lumen and a withdrawal lumen, and

said initial dialysis procedure performing step includes the steps of (i) advancing blood from a proximal end of said conduit toward a distal end of said conduit through said advancement lumen, and (ii) withdrawing blood from said distal end of said conduit toward said proximal end of said conduit through said withdrawal lumen.

66. The method of claim **50**, wherein:

said conduit includes a distal working segment in which said distal working orifice is defined,

said distal working segment extends out of a distal guide orifice of said guide catheter so that said distal working orifice is positioned outside of said guide lumen during said initial dialysis procedure performing step, and

said distal working segment is positioned completely within said guide catheter such that said distal working orifice is positioned within said guide lumen while said distal orifice of said conduit is locked within said guide lumen of said guide catheter.

67. The method of claim **50**, wherein:

said guide catheter further has a proximal guide orifice, and

said conduit extends through said proximal guide orifice, said guide lumen, and said distal guide orifice during said initial dialysis procedure performing step.

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